Ni(II)-catalyzed dehydrative alkynylation of unactivated (hetero)aryl C–H bonds using oxygen: an user-friendly approach

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Supporting Information

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1. General Information

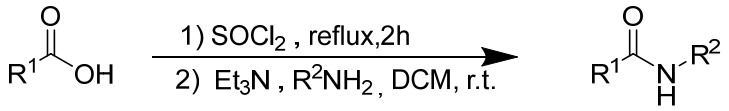
Trimethyacetonitrile was dried by Sodium, distilled under reduced pressure and stored under nitrogen. $NiI_2$was obtained from *Alfa Aesar*®. The other materials and solvents were purchased from Adamas and other commercial suppliers and used without additional purification. NMR spectra were recorded on a Bruke Avance operating for ^1H NMR at 400 MHz, ^{13}C NMR at 100 MHz using TMS as internal standard. The peaks were internally referenced to TMS (0.00 ppm) or residual undeuterated solvent signal (77.16 ppm for ^{13}C NMR).The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, b = broad. Mass spectroscopy data of the products were collected on an HRMS-TOF instrumentor a low-resolution MS instrument using EI ionization.

2. Experimental Section

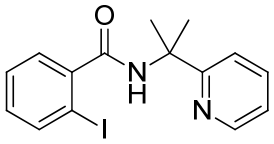
2.1 Preparation of Substrates

Compounds **1a-1z**, ***d*$_5$-1m**, **5a** were known compounds.[1-6] Compounds **4a** were prepared following typical method A.

General Procedure for the Preparation of Starting Materials (Method A):



A solution of acid (5 mmol) was refluxed in 5 mL $SOCl_2$ for 2h and cooled to RT.The excess of $SOCl_2$ was removed under vacuum to give corresponding acid choloride. The acid choloride was then re-dissolved in 5 mL dry CH_2Cl_2 and addeddropwiseto a 20 mL dry CH_2Cl_2 solution containing amine (5 mmol) and Et_3N (10mmol) at 0 ^oC. After stirring for 6h at ambient temperature, the resulting mixture waswashed with brine, dried over $MgSO_4$, filtered and concentrated under reducedpressure.The residue was purified by flash chromatography to give the desiredproduct.

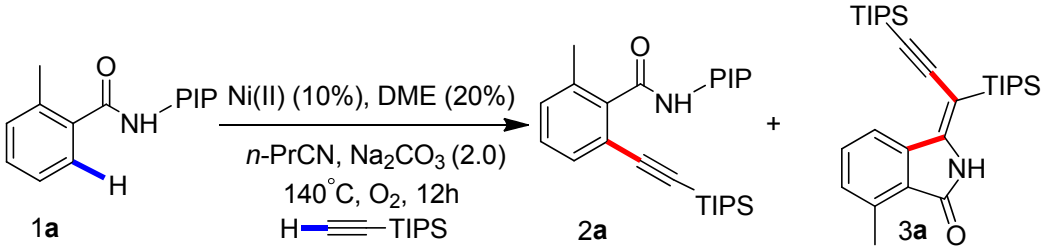


2-iodo-N-(2-(pyridin-2-yl)propan-2-yl)benzamide 4a

The title compound **4a** was prepared according to the general procedure (Method A). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 3.6 Hz, 1H), 8.19 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.51 – 7.43 (m, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.23 – 7.16 (m, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 1.91 (s, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.83, 164.41, 147.85, 143.73, 140.14, 137.52, 130.96, 128.45, 128.42, 122.29, 119.84, 92.97, 57.62, 27.73. **HRMS** (EI-TOF) calc.for$C_{15}H_{15}IN_2O(M^+)$:366.0229,found: 366.0233.

2.2 Optimization of Reaction Conditions

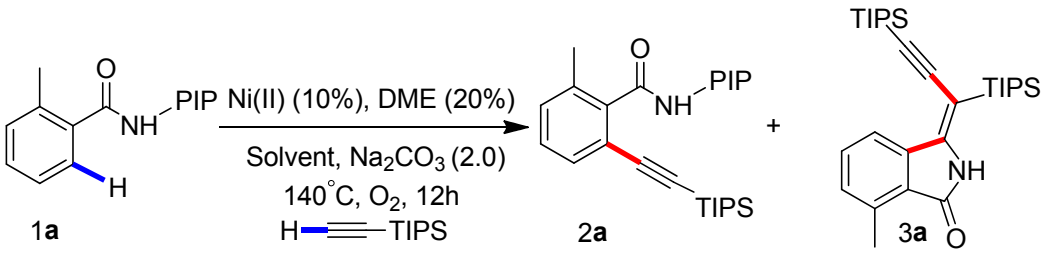
Screening of Ni Catalysts



Entry[a]	Ni(II)	Yield(%)[b] 2a/3a
1	$Ni(OTf)_2$	10/0
2	$Ni(acac)_2$	18/0
3	$Ni(OAc)_2$	19/0
4	NiI_2	37/0
5	$NiBr_2$	trace/0

[a] Reaction conditions unless noted: **1a (**0.1 mmol**),** alkyne (0.15 mmol), Ni(II) (0.01 mmol), DME (0.02 mmol), Na_2CO_3 (0.2 mmol), 1 atm O_2, *n*-PrCN (0.5 mL), 140°C, 12 h. [b] Dertimined by ^1H NMR analysis of the crude reaction mixtures using CH_2Br_2 as internal standard based on two parallel reactions.

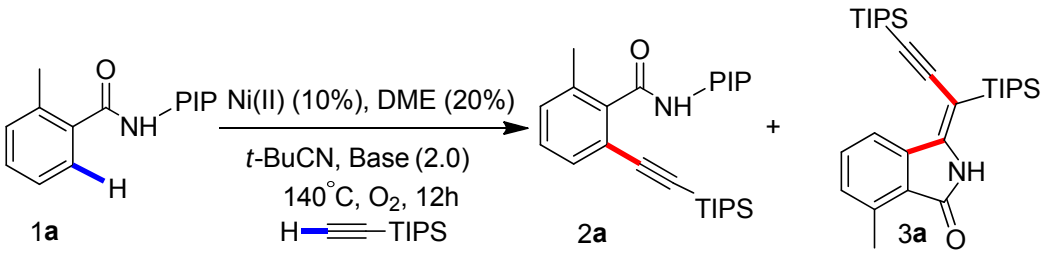
Screening of Solvents



Entry[a]	Solvent	Yield(%)[b] **2a**/**3a**
1	CH_2CN	0/0
2	*t*-BuCN	38/6
3	Toluene	28/0
4	*o*-xylene	0/0
5	DMSO	trace/0
6	DCE	trace/0

[a] Reaction conditions unless noted: **1a (**0.1 mmol**),** alkyne (0.15 mmol), Ni(II) (0.01 mmol), DME (0.02 mmol), Na_2CO_3 (0.2 mmol), 1 atm O_2, Solvent (0.5 mL), 140°C, 12 h. [b] Dertimined by ^1H NMR analysis of the crude reaction mixtures using CH_2Br_2 as internal standard based on two parallel reactions.

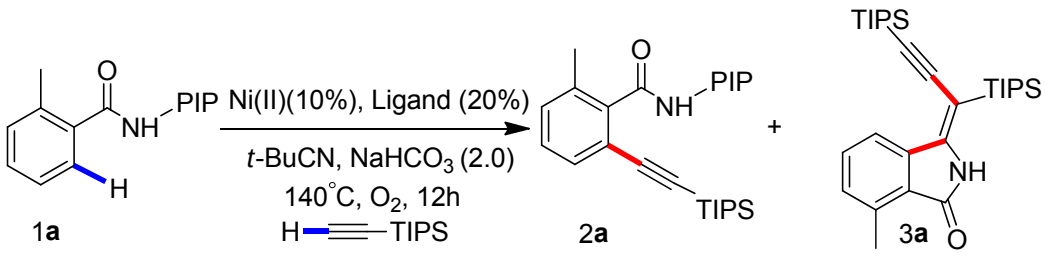
Screening of Bases



Entry[a]	Base	Yield(%)[b] **2a**/**3a**
1	Li_2CO_3	39/trace
2	$KHCO_3$	32/7
3	$NaHCO_3$	41/17
4	KH_2PO_4	47/20
5	LiOAc	32/7
6	NaOAc	trace/0
7	--	32/16
8	$NaHCO_3$:NaH_2PO_4=1:1	47/15
9	$NaHCO_3$:Li_2CO_3=1:1	45/16
10	$MgSO_4$	40/17
11	$CaCl_2$	44/14

[a] Reaction conditions unless noted: **1a (**0.1 mmol**),** alkyne (0.15 mmol), Ni(II) (0.01 mmol), DME (0.02 mmol), Base (0.2 mmol), 1 atm O_2, *t*-BuCN (0.5 mL), 140°C, 12 h. [b] Dertimined by ^{1}H NMR analysis of the crude reaction mixtures using CH_2Br_2 as internal standard based on two parallel reactions.

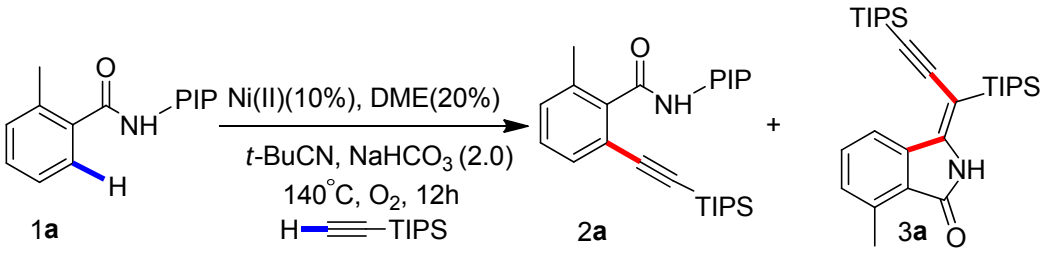
Screening of Ligands



Entry[a]	Ligand	Yield(%)[b] **2a**/**3a**
1	DME	41/17
2	DPPP	42/10
3	BINAP	47/17
4	1,10-Phen	<20/0
5	2,2'-Bipyridine	<20/0
6	BINOL	trace/0
7[c]	DME	41/5
8[c]	1,2-Dimethoxybenzene	48/5
9[c]	1,2-Bis(phenylthio)ethane	43/10
10[c]	S(*i*-Pr)$_2$	48/14
11[c]	SMe$_2$	34/trace
12[c]	COD	36/5
13[c]	18-Crown-6	45/trace
14[c]	digylme	32/trace

[a] Reaction conditions unless noted: **1a (**0.1 mmol**),** alkyne (0.15 mmol), Ni(II) (0.01 mmol), Ligand (0.02 mmol), $NaHCO_3$ (0.2 mmol), 1 atm O_2, *t*-BuCN (0.5 mL), 140°C, 12 h. [b] Dertimined by ^1H NMR analysis of the crude reaction mixtures using CH_2Br_2 as internal standard based on two parallel reactions.[c] alkyne (0.1 mmol).

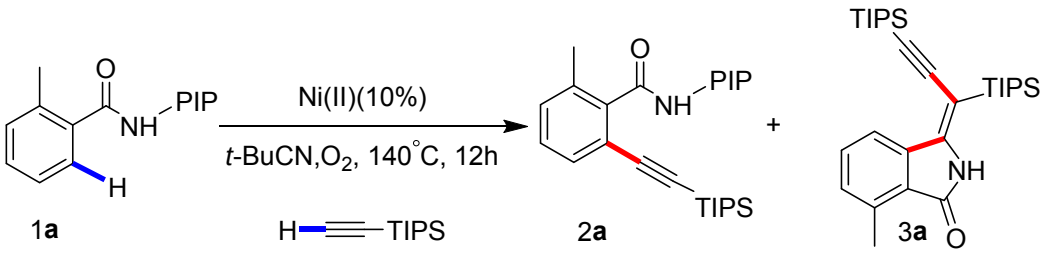
Screening of the equivalences of alkyne



Entry[a]	alkyne (mmol)	Yield(%)[b] **2a**/**3a**
1	0.5	40/7
2	1.0	38/4
3	1.5	40/9
4	2.0	42/13

[a] Reaction conditions unless noted: **1a (**0.1 mmol**),** alkyne (X mmol), Ni(II) (0.01 mmol), DME (0.02 mmol), $NaCO_3$ (0.2 mmol), 1 atm O_2, *t*-BuCN (0.5 mL), 140°C, 12 h. [b] Dertimined by ^1H NMR analysis of the crude reaction mixtures using CH_2Br_2 as internal standard based on **1a** of two parallel reactions.

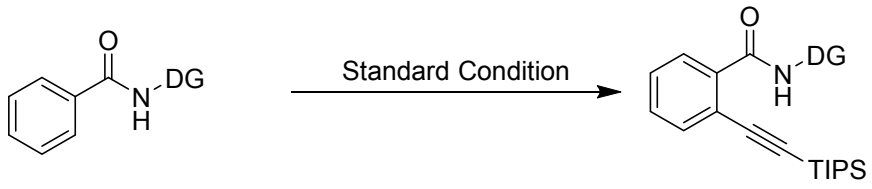
Influences of Bases, Ligands and equivalences of 1a

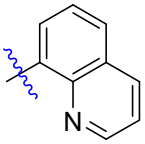
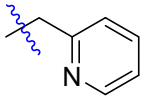
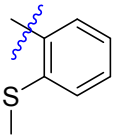
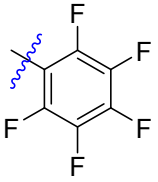


Entry[a]	$NaHCO_3$(mmol)	DME(mmol)	Yield(%)[b] **2a**/**3a**
1	0.2	0.02	40/7
2	0.2	0	53/6
3	0	0	52/6
4[c]	0	0	61/6
5[d]	0	0	73/6
6[d,f]	0	0	87[g]/trace
7[e,f]	0	0	87/trace

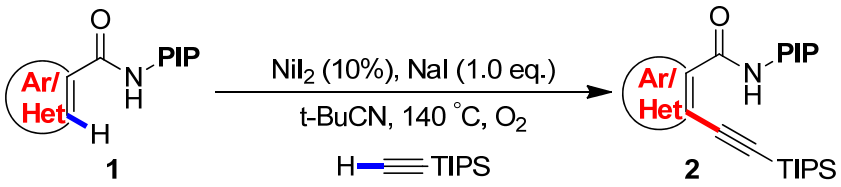
[a] Reaction conditions unless noted: **1a (**0.1 mmol**),** alkyne (0.1 mmol), Ni(II) (0.01 mmol), DME (0.02 mmol), $NaHCO_3$ (0.2 mmol), 1 atm O_2, *t*-BuCN (0.5 mL), 140°C, 12 h, two parallel reactions were conducted . [b] Dertimined by ^1H NMR analysis of the crude reaction mixtures using CH_2Br_2 as internal standard based on **alkyne**. c 1a (0.12 mmol). [d] 1a (0.15 mmol). [e] 1a (0.20 mmol). [f] 0.1mmol of NaI was added. [g] isolated yield.

Influences of Directing Group

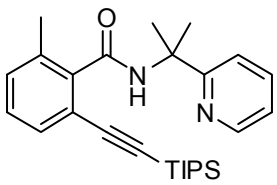


			
4, 37%	-	-	-

2.3 General Procedure for Alkynylation

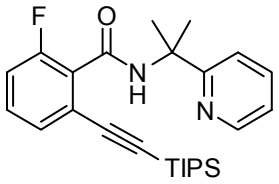


To an oven-dried 50 mL screw-capped vial was added substrate **1** (0.15 mmol), Triisopropylsilyacetylene (22.4 uL, 0.1 mmol), NiI_2 (3.12 mg, 0.01 mmol), NaI (14.9 mg, 0.1 mmol), *t*-BuCN (0.5 mL). Two parallel reactions were conducted. The mixture was stirred for 12 h (for aromatic amides) or 18 h (for heteroaromatic amides) at 140 °C under O_2 followed by cooling. Both resulting mixtures were diluted with 40ml dichloromethane, combined together, filtered through a celite pad and concentrated in vacuo. The residue was purified by flash chromatography using petroleum ether/ethyl acetate as the eluent to afford the product.



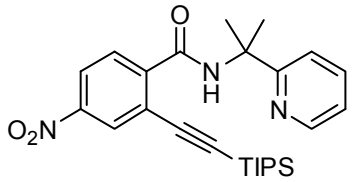
2-Methyl-N-(2-(Pyridin-2-yl)propan-2-yl)-6-((triisopropylsilyl)ethynyl)benzamide 2a[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.4 Hz, 1H), 8.15 (s, 1H), 7.71 (t, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.22 – 7.13 (m, 3H), 2.37 (s, 3H), 1.92 (s, 6H), 1.03 – 0.96 (m, 21H).



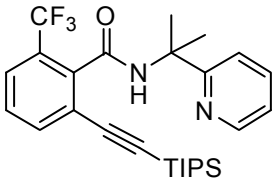
2-Fluoro-*N*-(2-(pyridin-2-yl)propan-2-yl)-6-((triisopropylsilyl)ethynyl)benzamide 2b[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.0 Hz, 1H), 8.28 (s, 1H), 7.72 (td, *J* = 8.0, 2.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.28 – 7.24 (m, 1H), 7.17 (d, *J* = 6.4, 4.8Hz, 1H), 7.07 (td, *J* = 8.4Hz, 0.8Hz, 1H), 1.90 (s, 6H), 1.05 – 0.98 (m, 21H).



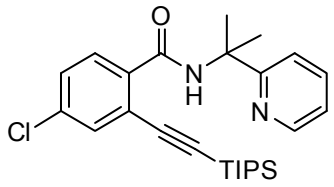
4-Nitro-*N*-(2-(pyridin-2-yl)propan-2-yl)-6-((triisopropylsilyl)ethynyl)benzamide 2c[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.48 (d, *J* = 4.4Hz, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.18 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.73 (td, *J* = 7.6, 1.2 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.20 (dd, *J* = 7.0, 5.0 Hz, 1H), 1.89 (s, 6H), 1.05 (s, 21H).



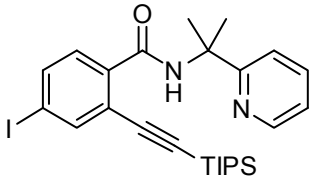
N-(2-(Pyridin-2-yl)propan-2-yl)-5-(trifluoromethyl)-2-((triisopropylsilyl)ethynyl) benzamide 2d[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.41 (d, *J* = 4.0 Hz, 1H), 7.72 (m, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.42 (m, 2H), 7.17 (dd, *J* = 6.8, 5.2 Hz, 1H), 1.91 (s, 6H), 1.03 – 0.97 (m, 21H).



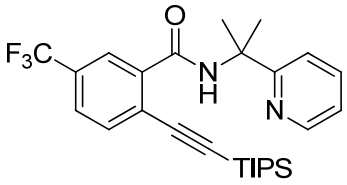
4-Chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)-6-((triisopropylsilyl)ethynyl)benzamide 2e[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.0 Hz, 1H), 8.43 (s, 1H), 7.74 – 7.66 (m, 2H), 7.51 (d, *J* = 1.5 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.34 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.16 (dd, *J* = 6.4, 4.8 Hz, 1H), 1.86 (s, 6H), 1.06 – 1.00 (m, 21H).



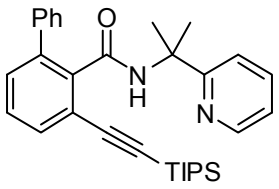
4-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)-6-((triisopropylsilyl)ethynyl)benzamide 2f

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.1 Hz, 1H), 8.42 (s, 1H), 7.88 (d, *J* = 1.6 Hz, 1H), 7.69 (m, 2H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.16 (dd, *J* = 6.8, 5.2 Hz, 1H), 1.85 (s, 6H), 1.06 – 1.00 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.56, 164.37, 147.98, 142.68, 137.65, 136.89, 130.49, 122.00, 121.71, 119.32 , 103.51, 98.88 , 95.50, 57.66 , 27.63, 18.63 , 11.27. **HRMS** (EI-TOF) calc. for$C_{26}H_{35}IN_2OSi$ (M^+): 546.1563, found: 546.1558.



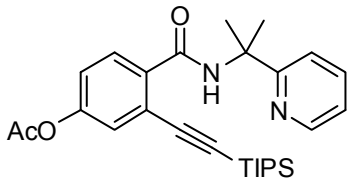
N-(2-(pyridin-2-yl)propan-2-yl)-5-(trifluoromethyl)-2-((triisopropylsilyl)ethynyl) benzamide 2g[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.50 (d, *J* = 4.8 Hz, 1H), 8.05 (s, 1H), 7.70 (td, *J* = 8.0, 2.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 6.9, 4.2 Hz, 1H), 1.88 (s, 6H), 1.12 – 0.96 (m, 21H).



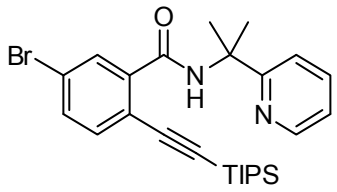
N-(2-(pyridin-2-yl)propan-2-yl)-3-((triisopropylsilyl)ethynyl)-[1,1'-biphenyl]-2-carboxamide 2h[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 4.0 Hz, 1H), 7.86 (s, 1H), 7.58 (td, *J* = 7.6, 1.4 Hz , 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 6.0 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 724 -7.31 (m, 4H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 7.2, 4.8 Hz, 1H), 1.59 (s, 6H), 1.13 – 0.93 (m, 21H).



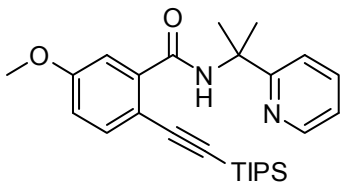
4-((2-(pyridin-2-yl)propan-2-yl)carbamoyl)-3-((triisopropylsilyl)ethynyl)phenyl acetate 2i

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.0 Hz, 1H), 8.41 (s, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.67 (td, , *J* = 8.0, 2.0 Hz 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.17 - 7.10 (m, 2H), 2.32 (s, 3H), 1.86 (s, 6H), 1.06 (s, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.99, 165.51, 164.45, 151.31, 148.01, 136.83, 135.74, 130.64, 127.20, 122.32, 121.65, 119.30, 104.21, 98.34, 77.37, 77.05, 76.73, 57.68, 27.69, 21.08, 18.63, 11.26. **HRMS** (EI-TOF) calc. for $C_{28}H_{38}N_2O_3Si$ (M^+): 478.2652, found: 478.2652.



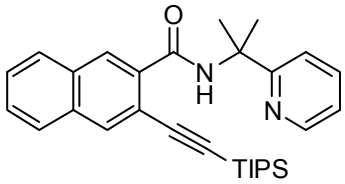
5-bromo-N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)benzamide 2j[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.0 Hz, 1H), 8.45 (s, 1H), 7.92 (d, *J* = 2.0 Hz, 1H), 7.69 (td, *J* = 7.6, 2.0 Hz, 1H), 7.48 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.16 (dd, *J* = 6.4, 6.2 Hz, 1H). 1.86 (s, 6H), 1.00 - 1.06 (m, 21H)



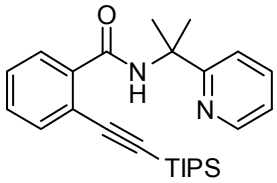
5-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)benzamide 2k

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.0 Hz, 1H), 8.47 (s, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.48 (m, 2H), 7.39 (s, 1H), 7.20 – 7.11 (m, 1H), 6.92 (dd, *J* = 8.2, 1.6 Hz, 1H), 3.82 (s, 3H), 1.86 (s, 6H), 1.27 – 0.97 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.71, 164.70, 159.93, 148.28, 138.76, 136.81, 136.44, 121.66, 119.41, 117.41, 113.43, 112.34, 105.70, 96.08, 57.93, 55.66, 27.94, 18.77, 11.43. **HRMS** (EI-TOF) calc.for $C_{27}H_{38}N_2O_2Si(M^+)$: 450.2703, found: 450.2701.



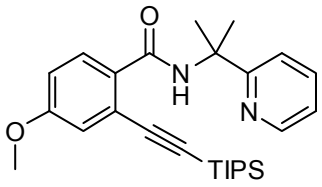
N-(2-(pyridin-2-yl)propan-2-yl)-3-((triisopropylsilyl)ethynyl)-2-naphthamide 2l[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.0 Hz, 1H), 8.48 (s, 1H), 8.32 (s, 1H), 8.09 (s, 1H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.69 (td, *J* = 7.9, 1.6 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.16 (dd, *J* = 6.4, 4.8 Hz, 1H), 1.91 (s, 6H), 1.11 – 1.00 (m, 21H).



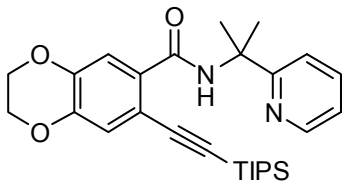
N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)benzamide 2m[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.4 Hz, 1H), 8.38 (s, 1H), 7.80 (dd, *J* = 6.4, 4.0 Hz, 1H), 7.67 (td, *J* = 8.0, 2.0 Hz, 1H), 7.57 (dd, *J* = 6.0, 2.8 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.15 (dd, *J* = 6.8, 5.6 Hz, 1H), 1.87 (s, 6H), 1.13 – 0.96 (m, 21H).



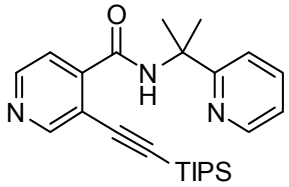
4-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)benzamide 2n[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.4 Hz, 1H), 8.32 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.65 (td, *J* =7.8, 1.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.13 (dd, *J* = 7.0, 5.4 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.84 (s, 3H), 1.84 (s, 6H), 1.13 – 1.00 (m, 21H).



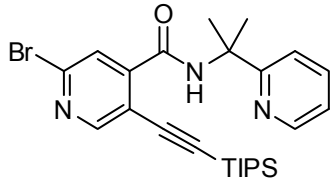
N-(2-(pyridin-2-yl)propan-2-yl)-7-((triisopropylsilyl)ethynyl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carboxamide 2o[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.0 Hz, 1H), 8.33 (s, 1H), 7.65 (td, *J* = 8.0, 1.6 Hz, 1H), 7.49 – 7.38 (m, 2H), 7.13 (dd, *J* = 7.0, 5.2 Hz, 1H), 7.05 (s, 1H), 4.26 (s, 4H), 1.83 (s, 6H), 1.11 – 1.01 (m, 21H).



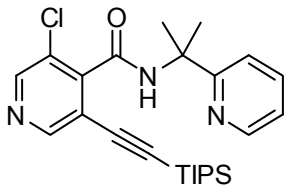
N-(2-(pyridin-2-yl)propan-2-yl)-3-((triisopropylsilyl)ethynyl)isonicotinamide 2p[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.60 (m, 2H), 8.49 (dd, *J* = 4.0, 0.8 Hz, 1H), 7.71 (td, *J* = 8.0, 1.76Hz, 1H), 7.63 (d, *J* = 4.8 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.14 (m, *J* = 6.6, 5.2 Hz1H), 1.87 (s, 6H), 1.15 – 0.94 (m, 21H).



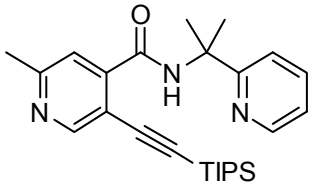
2-bromo-N-(2-(pyridin-2-yl)propan-2-yl)-5-((triisopropylsilyl)ethynyl)isonicotinamide 2q[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.51(s, 1H), 8.49 (d, *J* = 4.8 Hz, 1H), 7.79(s, 1H)7.73 (td,*J* = 7.6, 1.4 H 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.20 (dd, *J* = 7.0, 5.2 Hz, 1H), 1.86 (s, 6H), 1.16 – 0.95 (m, 21H).



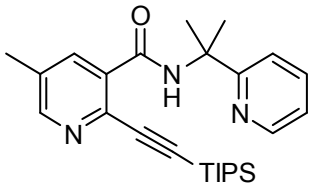
3-chloro-N-(2-(pyridin-2-yl)propan-2-yl)-5-((triisopropylsilyl)ethynyl)isonicotinamide 2r[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.56 (s, 1H), 8.54 (s, 1H), 8.44 (d, *J* = 4.4 Hz, 1H), 7.75 (td, *J* = 8.0, 1.6 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 6.8, 5.2 Hz, 1H), 1.92 (s, 6H), 0.97 -1.04 (m, 21H).



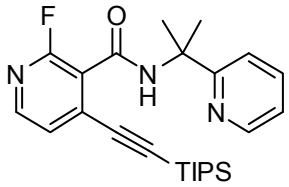
2-methyl-N-(2-(pyridin-2-yl)propan-2-yl)-5-((triisopropylsilyl)ethynyl)isonicotinamide 2s[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.56 (s, 1H), 8.50 (d, *J* = 4.4 Hz, 1H), 7.70 (td, *J* = 8.0, 1.6 Hz, 1H), 7.50 (s, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 7.2, 5.6 Hz, 1H), 2.58 (s, 3H), 1.86 (s, 6H), 1.12 – 0.91 (m, 21H).



5-methyl-N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)nicotinamide 2t[5]

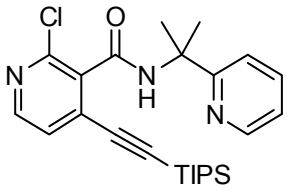
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.52 – 8.44 (m, 2H), 7.86 (s, 1H), 7.70 (td, *J* = 8.0, 2.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 7.2, 5.6 Hz, 1H), 2.36 (s, 3H), 1.87 (s, 6H), 1.21 – 0.93 (m, 21H).



2-fluoro-N-(2-(pyridin-2-yl)propan-2-yl)-4-((triisopropylsilyl)ethynyl)nicotinamide 2u

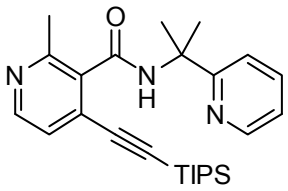
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.45 (d, *J* = 4.0 Hz, 1H), 8.16 (d, *J* = 4.8 Hz, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 4.8 Hz, 1H), 7.25 – 7.14 (m, 1H), 1.90 (s, 6H), 1.03 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.77, 160.15 (d, *J* = 237.6 Hz), 161.08 (d, *J* = 3.8 Hz), 158.97, 147.38, 147.26 (d, *J* = 16 Hz), 137.29, 133.51 (d, *J* = 5.8 Hz,), 125.44 (d, *J* = 4.3 Hz),

122.08 (d, *J* = 34.7 Hz), 122.00, 119.37, 102.72, 100.83 (d, *J* = 5.2 Hz), 57.51, 27.37, 18.52, 11.12. **HRMS** (EI-TOF) calc. for $C_{25}H_{34}FN_3OSi(M^+)$: 439.2455, found: 439.2449



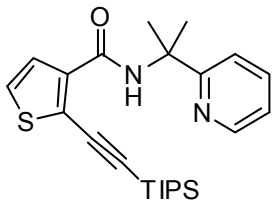
2-chloro-N-(2-(pyridin-2-yl)propan-2-yl)-4-((triisopropylsilyl)ethynyl)nicotinamide 2v[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.45 (d, *J* = 4.0 Hz, 1H), 8.33 (d, *J* = 4.8 Hz, 1H), 7.74 (td, *J* = 8.0, 1.6 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 5.2 Hz, 1H), 7.21 (dd, *J* = 6.8, 4.8 Hz, 1H), 1.92 (s, 6H), 1.01 - 1.05 (m, 21H).



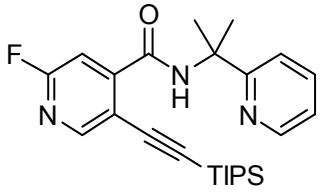
2-methyl-N-(2-(pyridin-2-yl)propan-2-yl)-4-((triisopropylsilyl)ethynyl)nicotinamide 2w

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.8 Hz, 2H), 8.39 (br, 1H), 7.74 (td, *J* = 8.0, 1.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.23 – 7.18 (m, 2H), 2.61 (s, 3H), 1.92 (s, 6H), 1.03 - 0.98 (m, 21H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.23, 164.07, 156.03, 148.63, 147.54, 137.33, 134.26, 128.77, 124.72, 122.09, 119.51, 102.39, 99.98, 57.33, 27.43, 22.70, 18.65, 11.27. **HRMS** (EI-TOF) calc. for$C_{26}H_{37}N_3OSi$ (M^+):435.2706, found: 435.2700



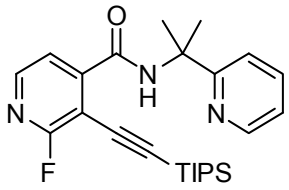
N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)thiophene-3-carboxamide 2x[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.0 Hz, 1H), 8.05 (s, 1H), 7.65 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 5.2 Hz, 1H), 7.10 - 7.15 (m, *J* = 6.4, 2H), 1.82 (s, 6H), 1.0 - 1.10 (m, 21H).



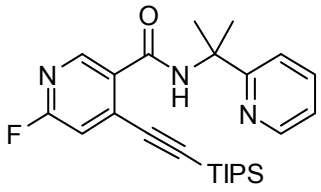
2-fluoro-N-(2-(pyridin-2-yl)propan-2-yl)-5-((triisopropylsilyl)ethynyl)isonicotinamide 2ya

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.49 (d, *J* = 4.0 Hz, 1H), 8.43 (s, 1H), 7.73 (td, *J* = 8.0, 1.6 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 2.0 Hz1H), 7.19 (dd, *J* = 6.8, 4.8 Hz, 1H), 1.87 (s, 6H), 1.14 – 0.93 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.72, 163.12 (d, *J* = 242.3Hz), 163.03 (d, *J* = 2.9 Hz), 152.18 (d, *J* = 14.7 Hz), 150.05 (d, *J* = 7.8 Hz), 147.89, 137.15, 121.99, 119.29, 114.82 (d, *J* = 5.1 Hz), 108.71 (d, *J* = 39 Hz), 100.27, 100.44, 57.81, 27.42, 18.57, 11.19. **HRMS** (EI-TOF) calc. for $C_{25}H_{34}FN_3OSi$ (M^+): 439.2455, found: 439.2449.



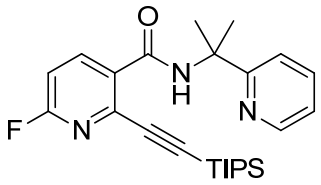
2-fluoro-N-(2-(pyridin-2-yl)propan-2-yl)-3-((triisopropylsilyl)ethynyl)isonicotinamide 2yb[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.49 (d, *J* = 4.0 Hz, 1H), 8.18 (d, *J* = 5.2 Hz, 1H), 7.73 (td, *J* = 8.0, 1.6 Hz, 1H), 7.50 (d, *J* = 5.2 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.20 (dd, *J* = 6.4, 5.0 Hz, 1H), 1.88 (s, 6H), 1.04 (s, 21H).



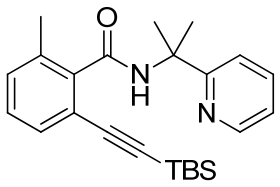
6-fluoro-N-(2-(pyridin-2-yl)propan-2-yl)-4-((triisopropylsilyl)ethynyl)nicotinamide 2za

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.54 (s, 1H), 8.49 (d, *J* = 4.4 Hz, 1H), 7.73 (td, *J* = 8.0, 1.6 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 6.6, 5.0 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 1.87 (s, 6H), 1.13 – 0.94 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.02, 163.54, 163.98 (d, *J* = 240.4 Hz), 149.13 (d, *J* = 16.3 Hz), 147.80 , 137.18, 133.46 (d, *J* = 9.8 Hz), 131.40 (d, *J* = 4.8 Hz,), 121.95, 119.36, 113.20(d, *J* = 38.4 Hz), 104.54, 101.28 (d, *J* = 3.9 Hz), 57.63, 27.48, 18.54, 11.15. **HRMS** (EI-TOF) calc. for $C_{25}H_{34}FN_3OSi(M^+)$: 439.2455, found: 439.2448.



6-fluoro-N-(2-(pyridin-2-yl)propan-2-yl)-2-((triisopropylsilyl)ethynyl)nicotinamide 2zb

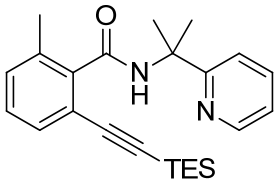
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.50 (d, *J* = 4.4 Hz, 1H), 8.16 (t, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.15 (m, 1H), 6.94 (dd, *J* = 8.4, 2.8 Hz, 1H), 1.87 (s, 6H), 1.20 – 0.93 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.05, 164.01, 162.78 (d, *J* = 242.9 Hz), 147.94, 142.72 (d, *J* = 8.7 Hz,), 137.37 (d, *J* = 16.5 Hz), 137.0, 132.84 (d, *J* = 4.5 Hz), 121.89, 119.30, 109.81(d, *J* = 37.4 Hz), 102.99, 99.27, 57.73, 27.50, 18.59, 11.26. **HRMS** (EI-TOF) calc. for $C_{25}H_{34}FN_3OSi(M^+)$: 439.2455, found: 439.2449.



2-((tert-butyldimethylsilyl)ethynyl)-6-methyl-N-(2-(pyridin-2-yl)propan-2-yl)benzamide 4a

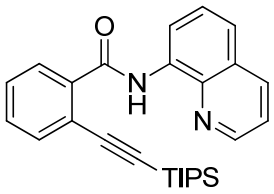
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.8 Hz, 1H), 8.12 (s, 1H), 7.72 (td, *J* = 7.6, 1.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 6.8 Hz, 1H), 7.22 – 7.12 (m, 3H), 2.38 (s, 3H), 1.92 (s, 6H), 0.91 (s, 9H), 0.03 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.63, 164.49, 147.63, 140.37, 137.15, 135.66,

130.95, 130.68, 128.32, 121.92, 120.37, 119.59, 103.77, 95.82, 77.48, 77.16, 76.84, 57.31, 27.62, 26.23, 19.51, 16.84, -4.61. **HRMS** (EI-TOF) calc. for C24H32N2OSi (M^+) :392.2284, found: 392.2279



2-methyl-N-(2-(pyridin-2-yl)propan-2-yl)-6-((triethylsilyl)ethynyl)benzamide 4b

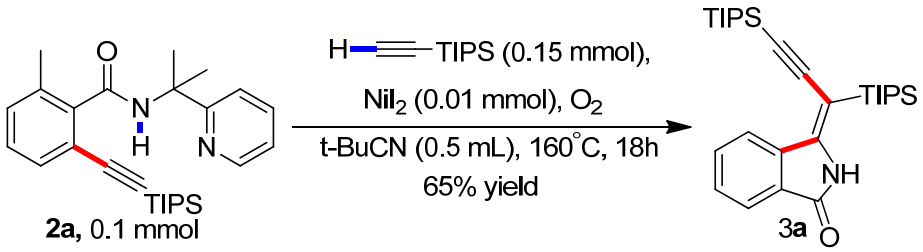
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 3.6 Hz, 1H), 8.10 (s, 1H), 7.72 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.23 – 7.06 (m, 3H), 2.37 (s, 3H), 1.92 (s, 6H), 0.92 (t, *J* = 7.8 Hz, 9H), 0.55 (q, *J* = 8.0 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.69, 164.50, 147.64, 140.38, 137.12, 135.61, 131.04, 130.62, 128.30, 121.91, 120.42, 119.58, 104.28, 95.05, 77.48, 76.84, 57.30, 27.55, 19.47, 7.52, 4.43. **HRMS** (EI-TOF) calc. for C24H32N2OSi (M^+) :392.2284, found: 392.2276



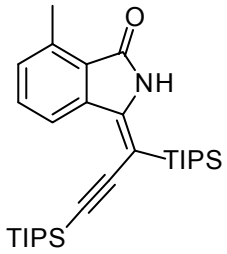
N-(quinolin-8-yl)-2-((triisopropylsilyl)ethynyl)benzamide 5

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 8.92 (d, *J* = 7.2 Hz, 1H), 8.76 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.80 (dd, *J* = 5.4, 3.4 Hz, 1H), 7.66 – 7.51 (m, 3H), 7.48 – 7.39 (m, 3H), 0.80 - 0.84 (m, 21H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.44, 148.25, 139.26, 138.92, 136.19, 134.69, 133.91, 130.12, 128.68, 127.92, 127.36, 121.85, 121.46, 120.76, 117.15, 103.88, 97.16, 18.31, 11.07. **HRMS** (EI-TOF) calc. for $C_{27}H_{32}N_2OSi(M^+)$:428.2284, found: 428.2280.

2.4 Procedure for Intramolecular Aminoalkynylation of 2a



To an oven-dried 50 mL screw-capped vial was added **2a** (0.10mmol), Triisopropylsilyacetylene (34 uL, 0.15 mmol), NiI_2 (3.12 mg, 0.01 mmol), *t*-BuCN (0.5 mL). The mixture was stirred for 18 h at 160 °C under O_2 followed by cooling. The resulting mixture was diluted with 40 mL dichloromethane, filtered through a celite pad and concentrated in vacuo. The residue was purified by preparative TLC using petroleum ether/ethyl acetate as the eluent to afford the product.



(Z)-3-(1, 3-bis(triisopropylsilyl)prop-2-yn-1-ylidene)-7-methylisoindolin-1-one 3a

^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 9.02 (d, *J* = 8.0 Hz, 1H), 7.99 (s, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 1H), 2.66 (s, 3H), 1.84 – 1.65 (m, 3H), 1.34 – 0.99 (m, 39H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.59, 148.96, 137.66, 137.54, 132.18, 126.30, 123.36, 108.23, 103.22, 98.56, 77.48, 77.16, 76.84, 18.81, 18.80, 17.72, 12.95, 11.80, 1.16. **HRMS** (EI-TOF) calc. for $C_{30}H_{49}NOSi_2$ (M^+): 495.3353, found: 495.3352.

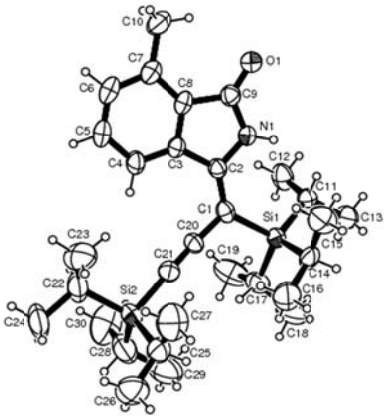


Figure 1. ORTEP diagram of compound 3a.

Bond precision: C-C = 0.0135 A Wavelength=0.71073

Cell: a=12.5020(8) b=15.8137(9) c=17.4136(10)

alpha=74.497(2) beta=75.487(1) gamma=76.750(2)

Temperature: 296 K

	Calculated	Reported
Volume	3162.7(3)	3162.7(3)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C30 H49 N O Si2	?
Sum formula	C30 H49 N O Si2	C30 H49 N O Si2
Mr	495.88	495.88
Dx,g cm-3	1.041	1.041
Z	4	4

Mu (mm-1)	0.133	0.133
F000	1088.0	1088.0
F000’	1088.97	
h,k,lmax	14,18,20	14,18,20
Nref	11150	11075
Tmin,Tmax	0.944,0.963	0.943,0.964
Tmin’	0.942	

Correction method= # Reported T Limits: Tmin=0.943 Tmax=0.964

AbsCorr = MULTI-SCAN

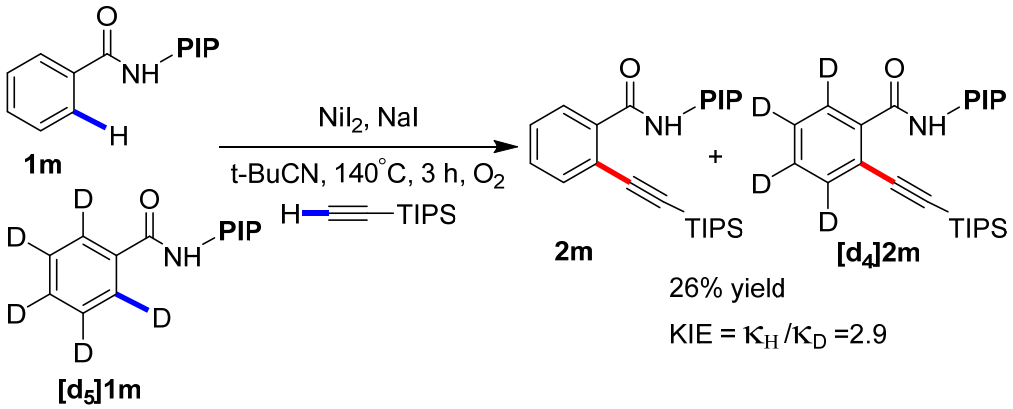
Data completeness= 0.993 Theta(max)= 25.000

R(reflections)= 0.1479 (5124) wR2(reflections)= 0.4410 (11075)

S = 1.191 Npar= 569

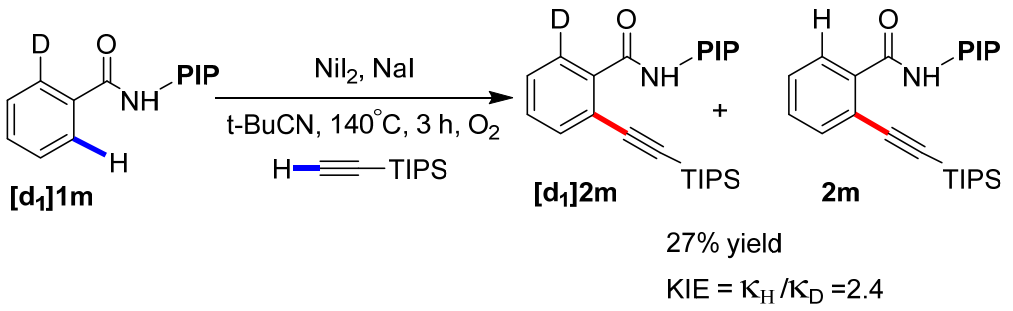
2.5 Mechanism Investigation

Intermolecular Competition KIE



To an oven-dried 50 mL screw-capped vial was added substrate **1m** (0.075mmol), ***d*$_5$-1m** (0.075mmol), Triisopropylsilyacetylene (22.4 uL, 0.1mmol), NiI_2 (3.12 mg, 0.01mmol), NaI (14.9 mg, 0.1 mmol), *t*-BuCN (0.5 mL). The mixture was stirred for 3h at 140 °C under O_2 followed by cooling. The resulting mixture was diluted with 40mL dichloromethane, filtered through a celite pad and concentrated in vacuo. The residue was purified by preparative TLC using petroleum ether/ethyl acetate as the eluent to afford the product. The ratio of product **2m/[d$_4$]2m** was determined by ^{1}H NMR analysis using CH_2Br_2 as internal standard.

Intramolecular Competition KIE



To an oven-dried 50 mL screw-capped vial was added substrate ***o*-d-1m** (0.15mmol), Triisopropylsilyacetylene (22.4 uL, 0.1mmol), NiI_2 (3.12 mg, 0.01mmol), NaI (14.9 mg, 0.1 mmol), *t*-BuCN (0.5 mL). The mixture was stirred for 3h at 140 °C under O_2

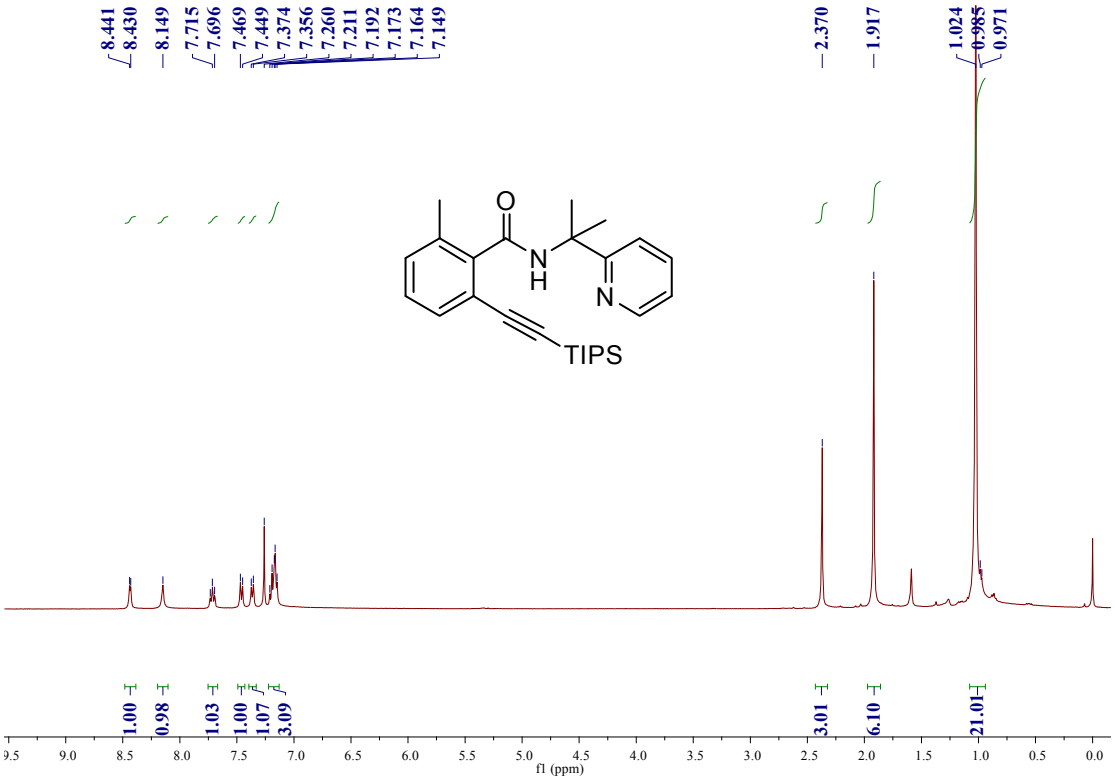
followed by cooling. The resulting mixture was diluted with 40mL dichloromethane, filtered through a celite pad and concentrated in vacuo. The residue was purified by preparative TLC using petroleum ether/ethyl acetate as the eluent to afford the product. The ratio of product **[d_1]2m/2m** was determined by ^{1}H NMR analysis using CH_2Br_2 as internal standard.

3. References

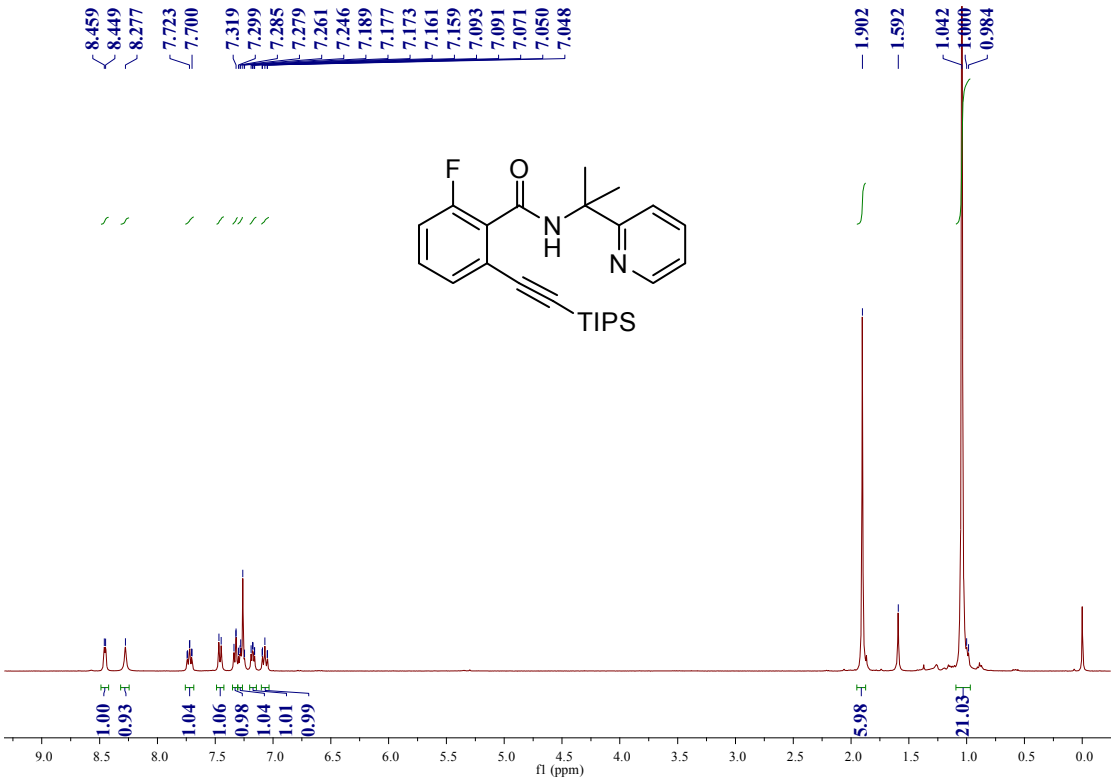
1. Y. Aihara, N. Chatani, *J. Am. Chem. Soc.,* 2013, **135**, 5308.
2. F.-J. Chen, G. Liao, X. Li, J. Wu, B.-F. Shi, *Org. Lett.,* 2014, **16**, 5644.
3. X. Li, Y.-H. Liu, Yan-Hua, W.-J. Gu, B. Li, F.-J. Chen, B.-F. Shi, *Org. Lett.,* 2014, **16**, 3904.
4. B. Li, B. Liu, B.-F. Shi, *Chem. Commun.,* 2015, **51**, 5093.
5. Y.-J. Liu, Y.-H. Liu, S.-Y. Yan, B.-F. Shi, *Chem. Commun.,* 2015, **51**, 6388.
6. Y.-J. Liu, Y.-H. Liu, X.-S. Yin, W.-J. Gu and B.-F. Shi, *Chem. Eur. J.*, 2015, **21**, 205.

4. NMR Spectra

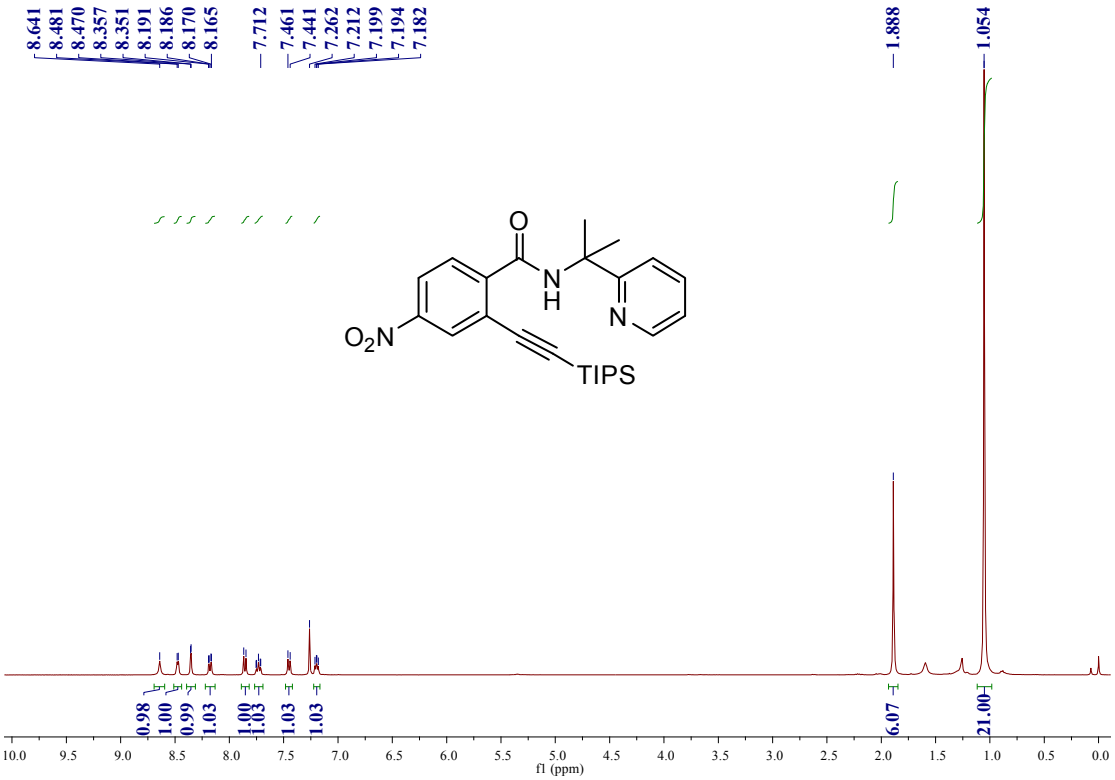
2a



2b



2c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8.351
8.191
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8.170
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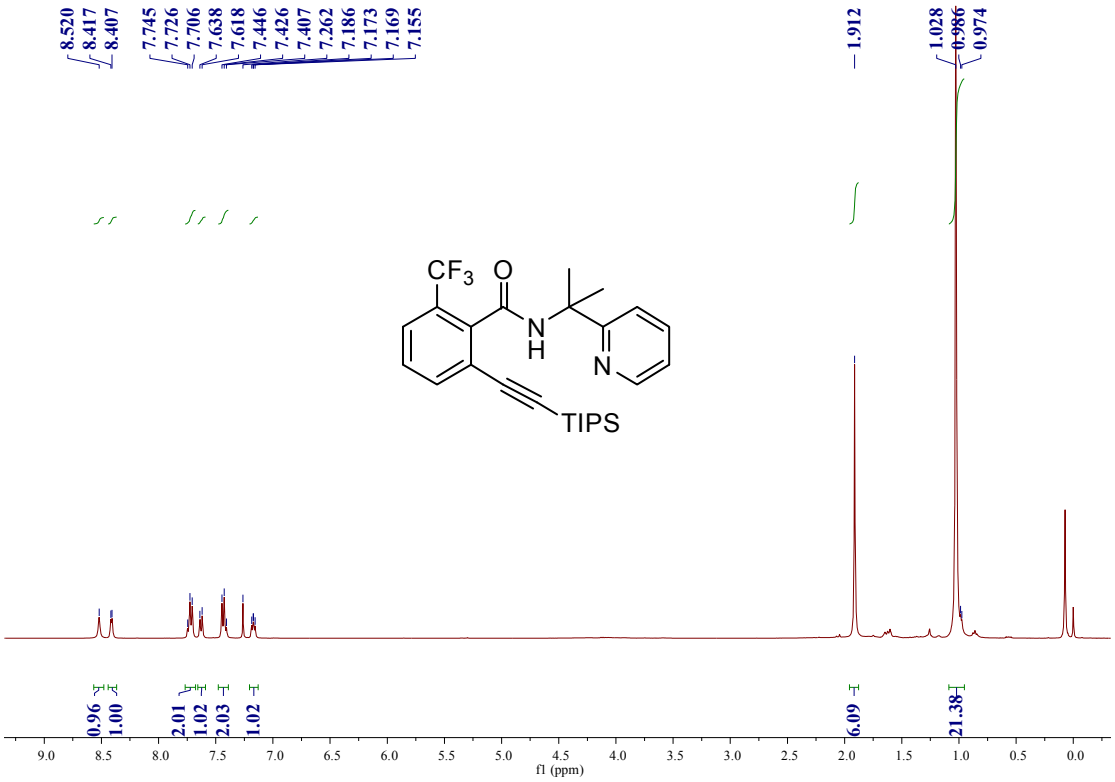
7.712
7.461
7.441
7.262
7.212
7.199
7.194
7.182
1.888
1.054
O
N
H
N
O_2N
TIPS
0.98
1.00
0.99
1.03
1.00
1.03
1.03
1.03
6.07
21.00
f1 (ppm)

2d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7.706
7.638
7.618
7.446
7.426
7.407
7.262
7.186
7.173
7.169
7.155
1.912
1.028
0.986
0.974
CF_3
O
N
H
N
TIPS
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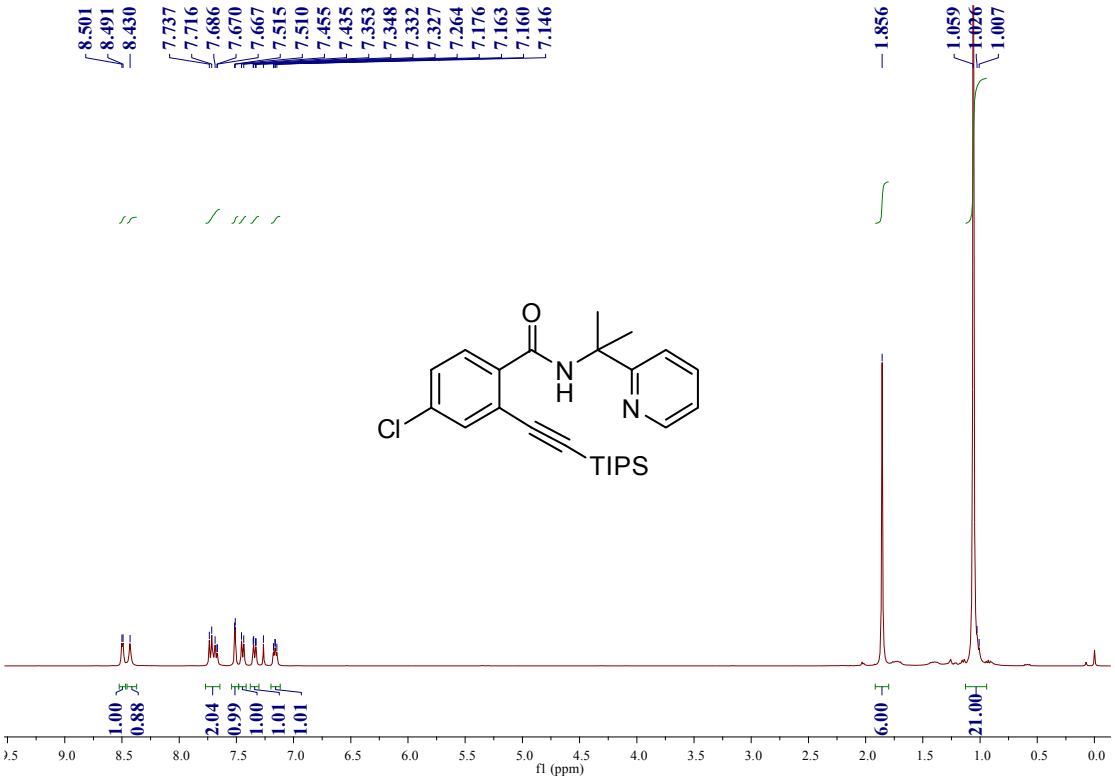
2.01
1.02
2.03
1.02
6.09
21.38
f1 (ppm)

2e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8.491
8.430
7.737
7.716
7.686
7.670
7.667
7.515
7.510
7.455
7.435
7.353
7.348
7.332
7.327
7.264
7.176
7.163
7.160
7.146
1.856
1.059
1.026
1.007
O
N
H
N
Cl
TIPS
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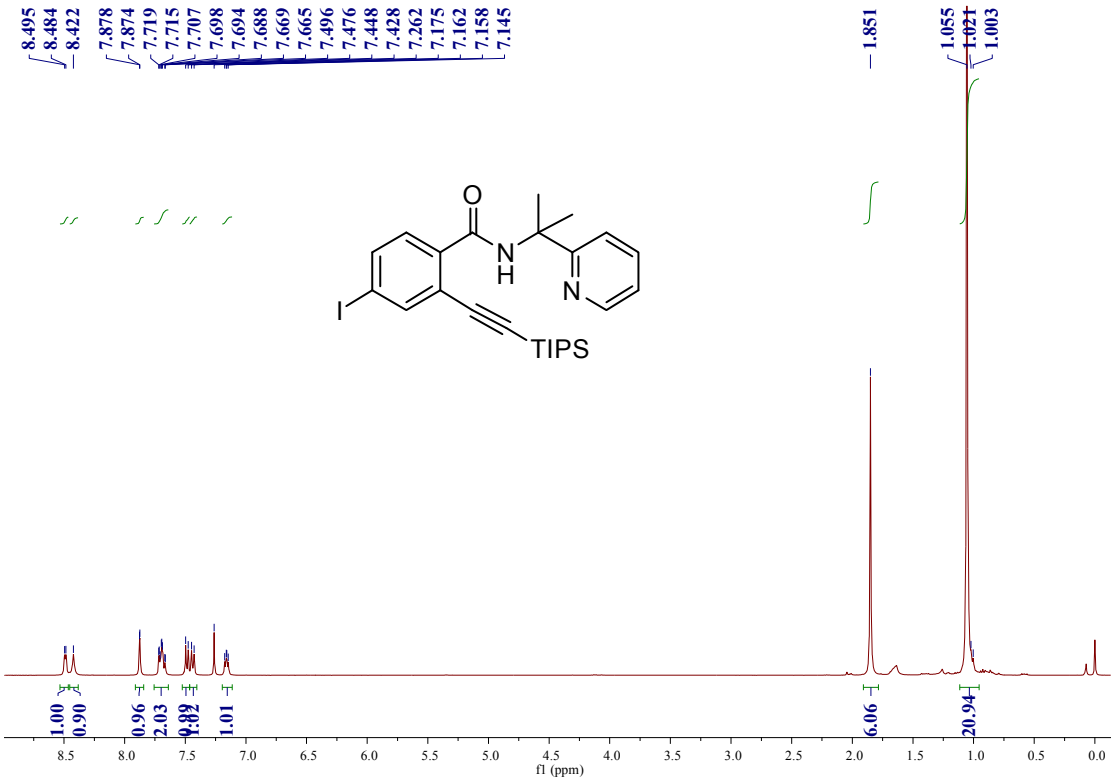
2.04
0.99
1.00
1.01
1.01
6.00
21.00
f1 (ppm)

2f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8.422
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7.874
7.719
7.715
7.707
7.698
7.694
7.688
7.669
7.665
7.496
7.476
7.448
7.428
7.262
7.175
7.162
7.158
7.145
1.851
1.055
1.021
1.003
O
N
H
N
I
TIPS
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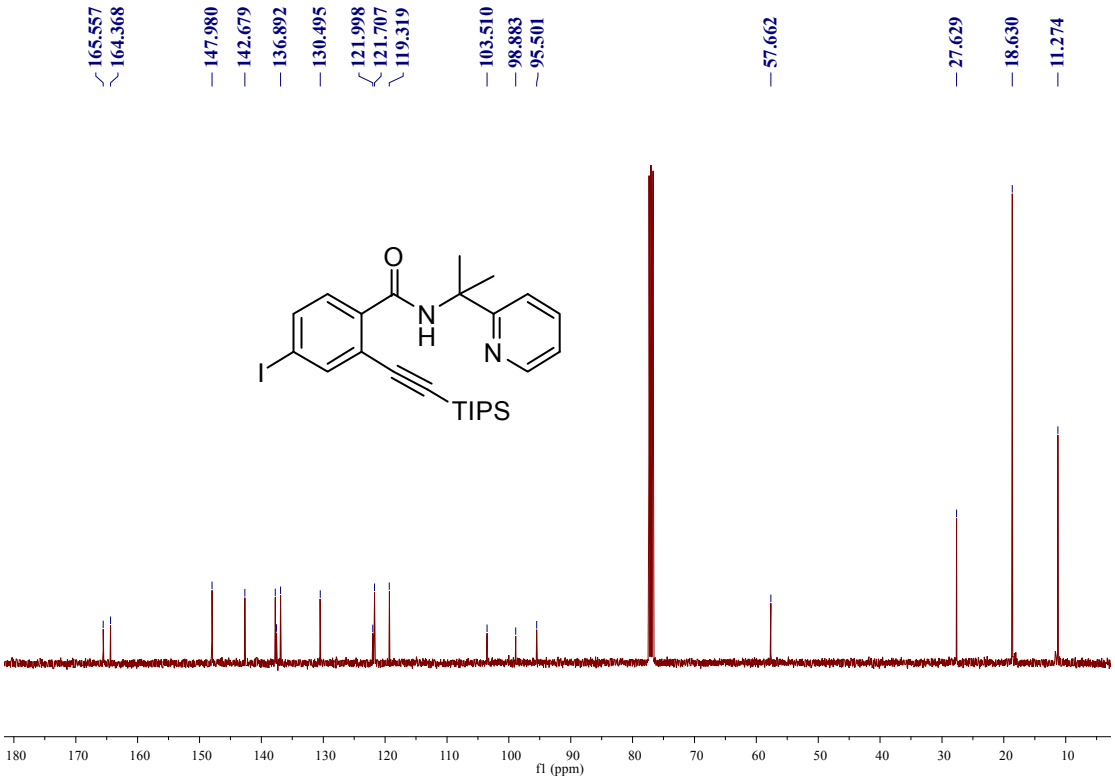
0.96
2.03
1.01
6.06
20.94
f1 (ppm)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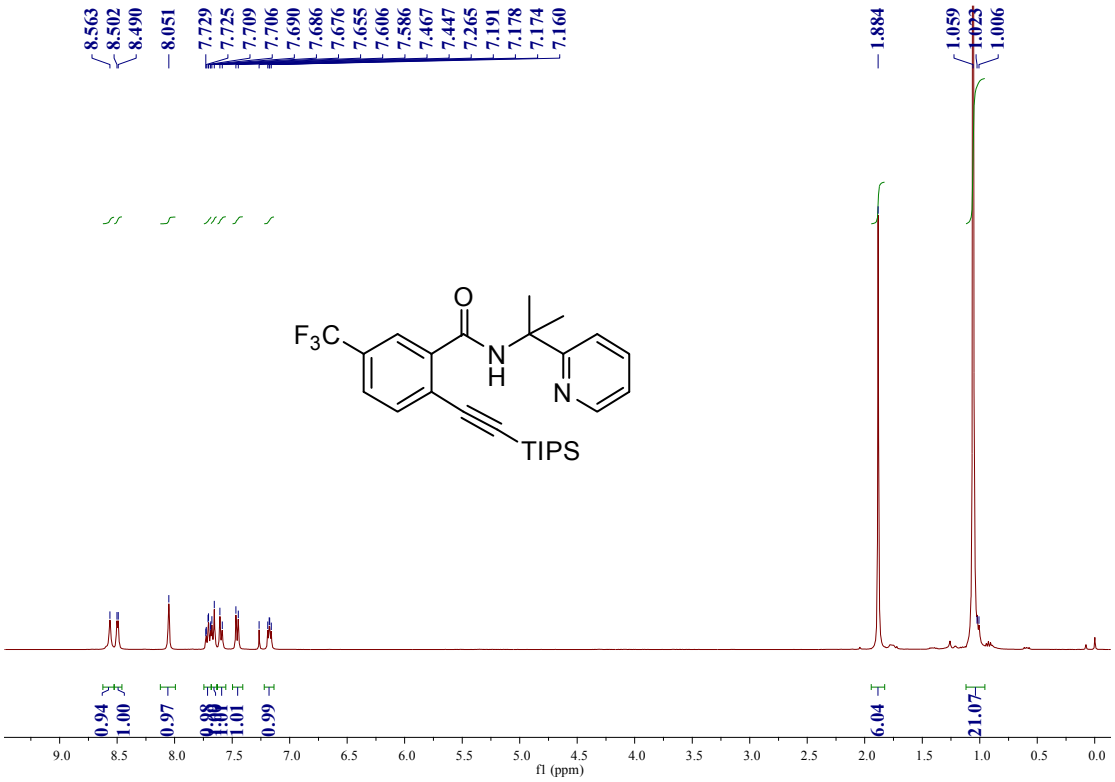
164.368
147.980
142.679
136.892
130.495
121.998
121.707
119.319
103.510
98.883
95.501
57.662
27.629
18.630
11.274
O
N
H
N
I
TIPS
f1 (ppm)

2g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8.051
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7.725
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7.706
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7.606
7.586
7.467
7.447
7.265
7.191
7.178
7.174
7.160
1.884
1.059
1.023
1.006
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F3C
N
H
N
TIPS
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0.99
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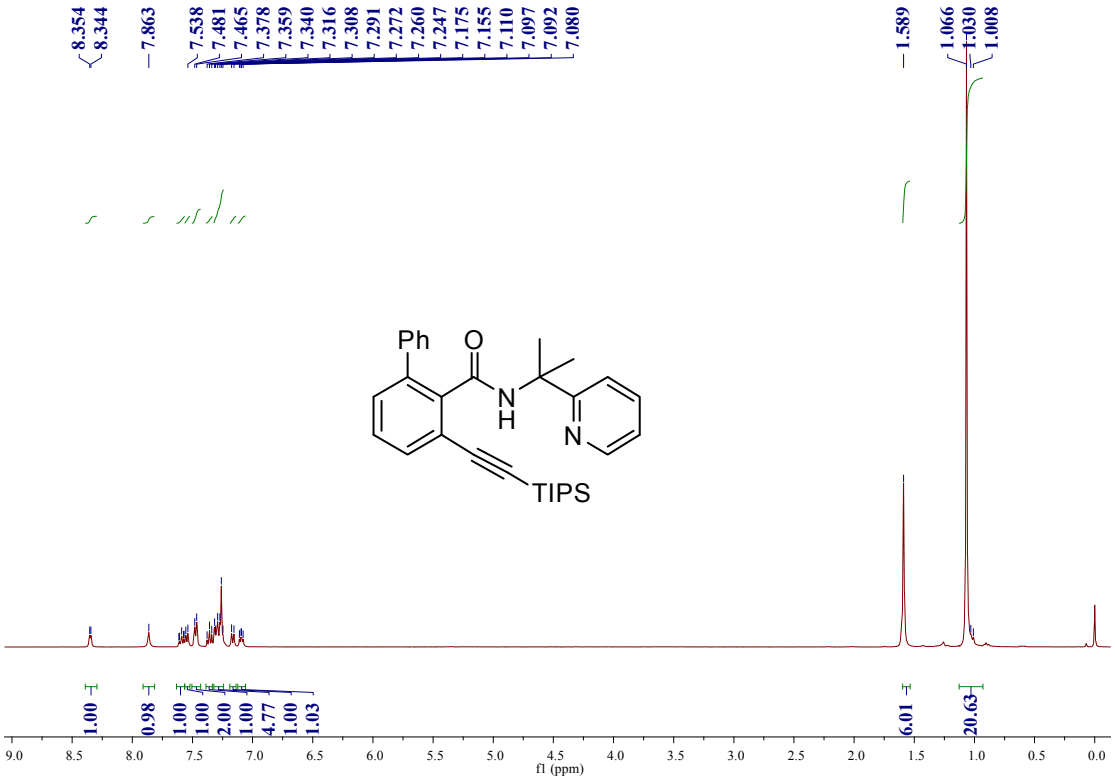
21.07
f1 (ppm)

2h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7.272
7.260
7.247
7.175
7.155
7.110
7.097
7.092
7.080
1.589
1.066
1.030
1.008
Ph
O
N
H
N
TIPS
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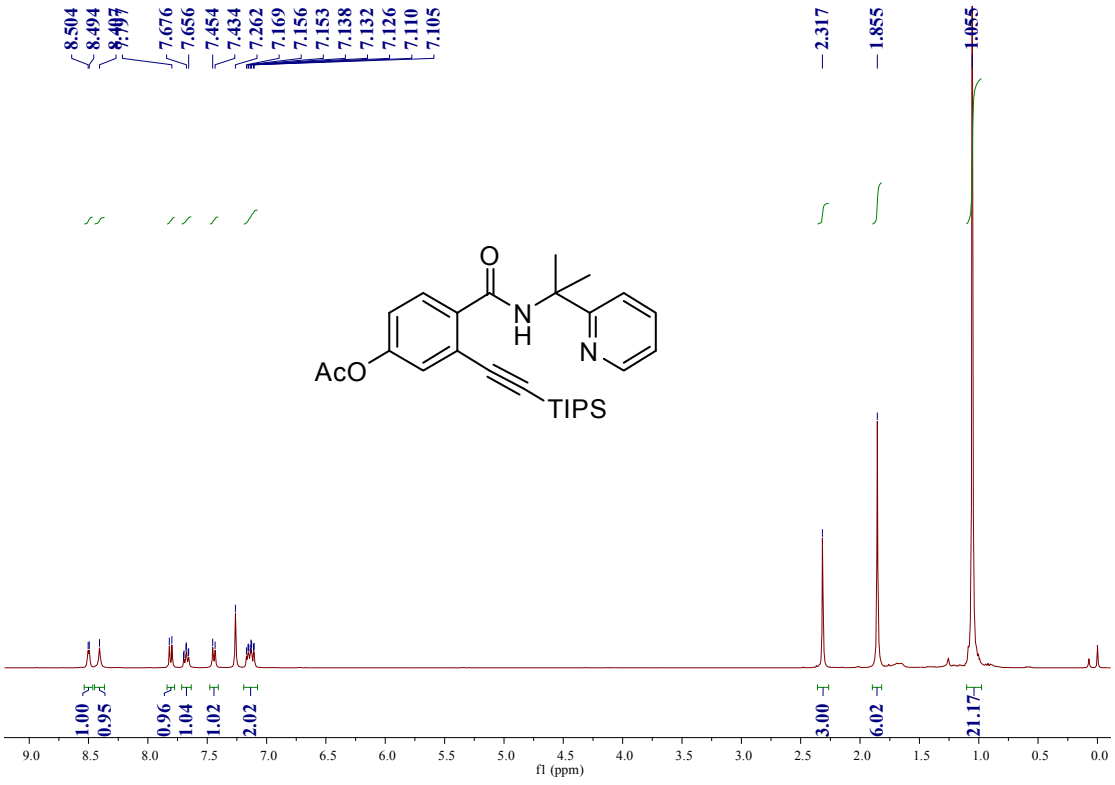
1.03
6.01
20.63
f1 (ppm)

2i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7.126
7.110
7.105
2.317
1.855
1.055
O
N
H
N
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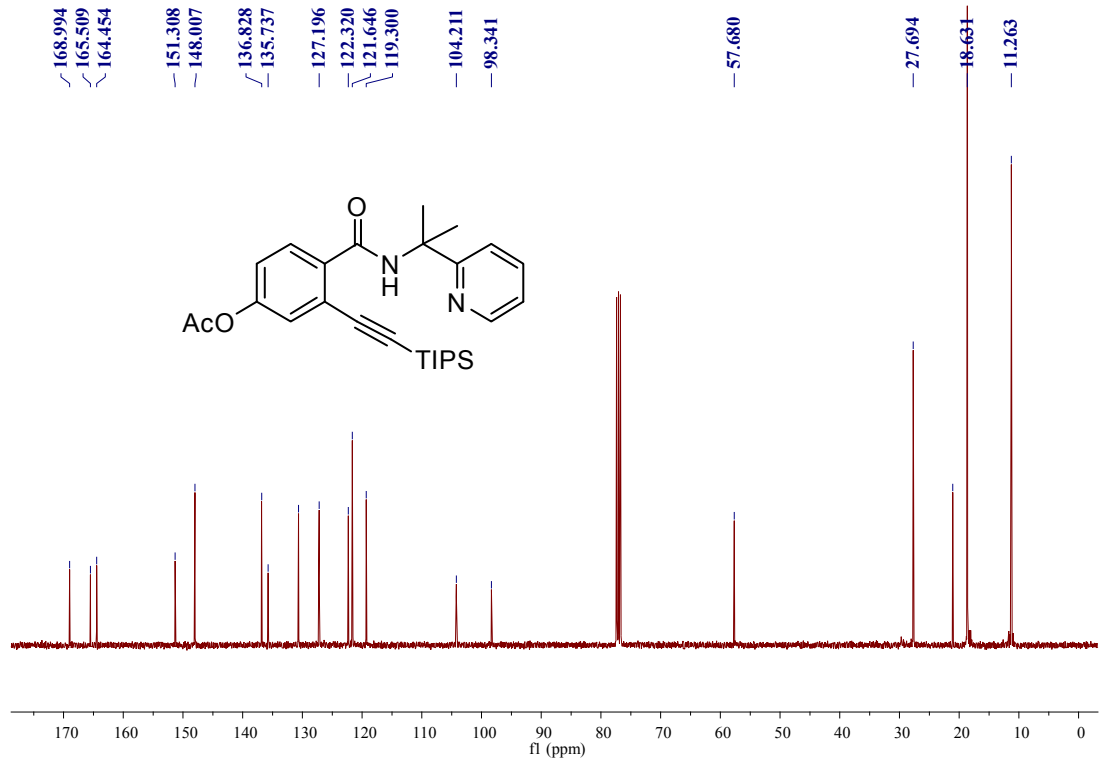
f1 (ppm)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127.196
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121.646
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104.211
98.341
57.680
27.694
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11.263
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N
H
N
AcO
TIPS
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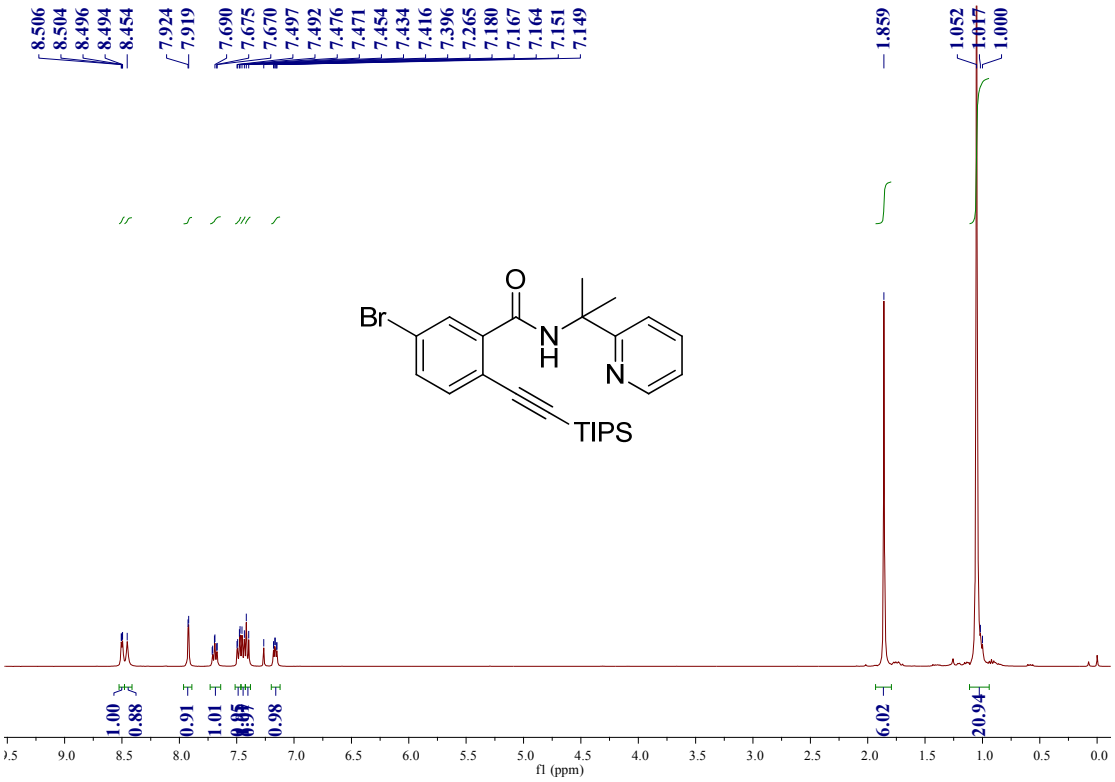
f1 (ppm)

2j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8.494
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7.476
7.471
7.454
7.434
7.416
7.396
7.265
7.180
7.167
7.164
7.151
7.149
1.859
1.052
1.017
1.000
Br
O
N
H
N
TIPS
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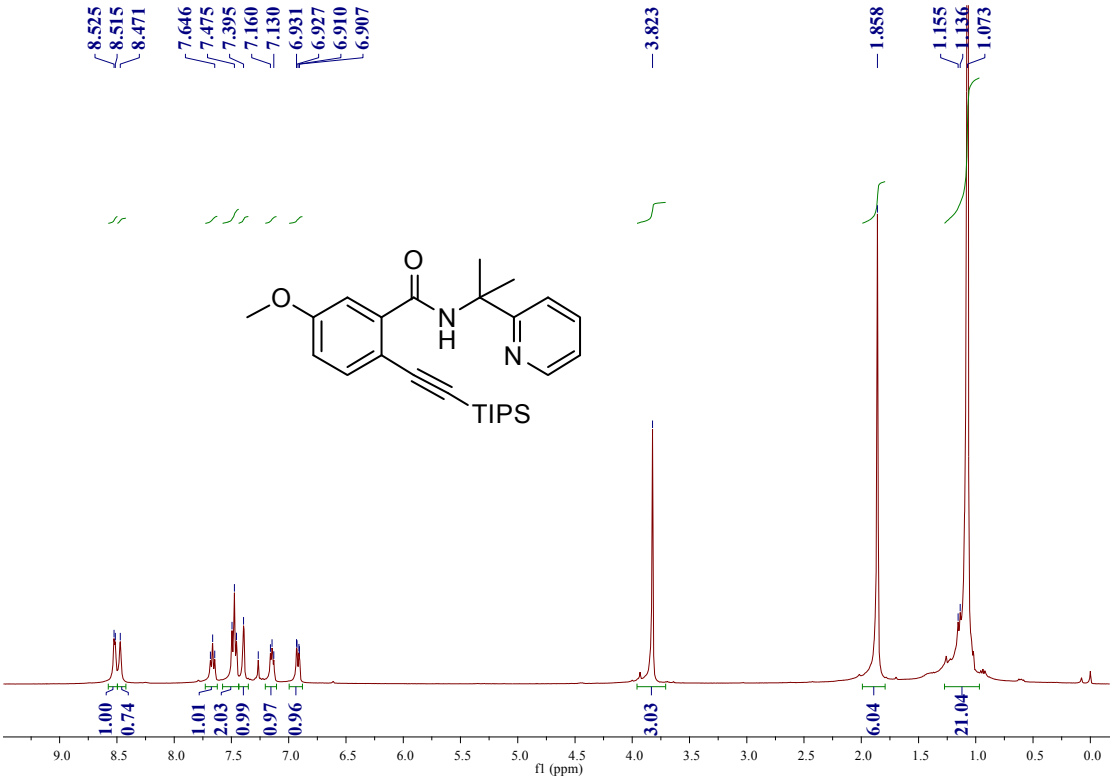
6.02
20.94
f1 (ppm)

2k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1.858
1.155
1.136
1.073
O
O
N
H
N
TIPS
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0.74
1.01
2.03
0.99
0.97
0.96
3.03
6.04
21.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
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2.5
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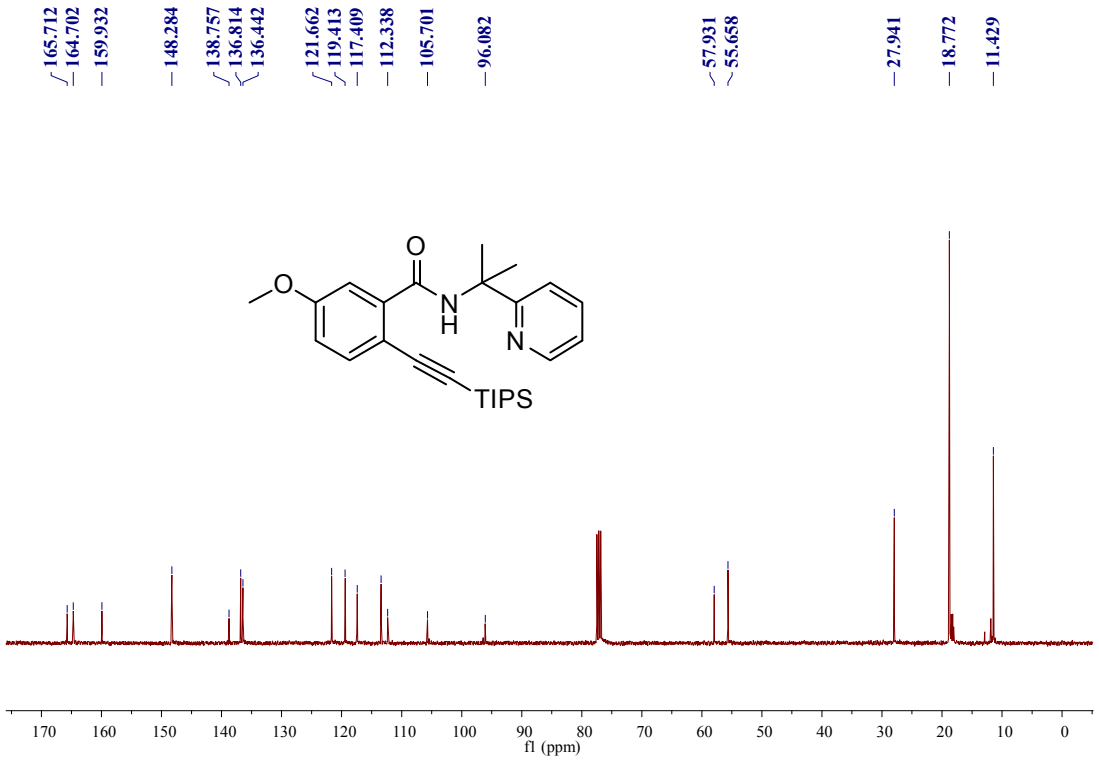
1.5
1.0
0.5
0.0
f1 (ppm)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57.931
55.658
27.941
18.772
11.429
O
O
N
H
N
TIPS
170
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150
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110
100
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70
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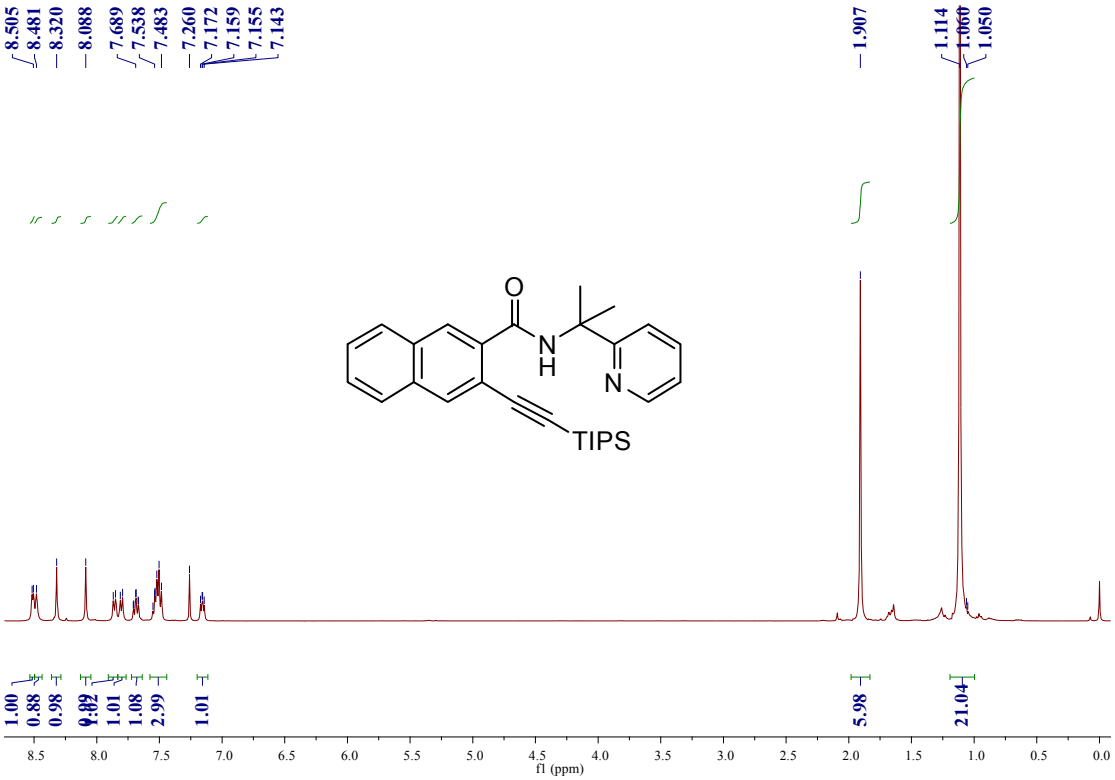
50
40
30
20
10
0
f1 (ppm)

2l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O
N
H
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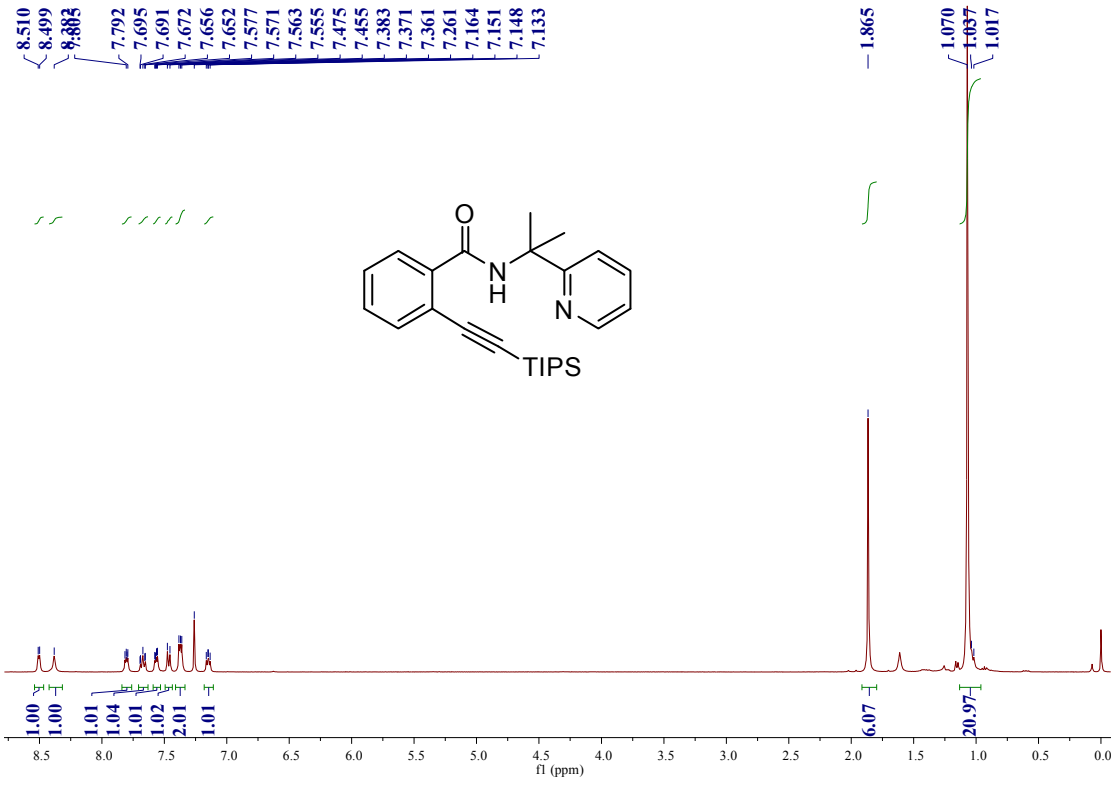
f1 (ppm)

2m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7.571
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7.475
7.455
7.383
7.371
7.361
7.261
7.164
7.151
7.148
7.133
1.865
1.070
1.037
1.017
O
N
H
N
TIPS
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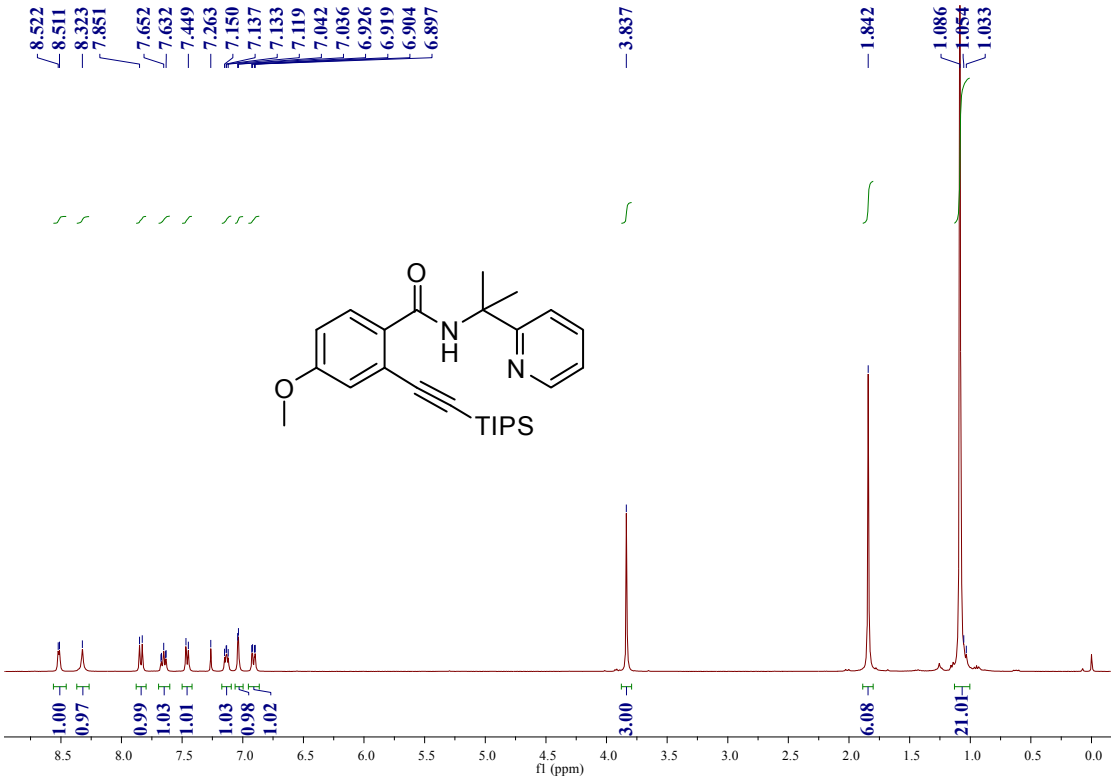
6.07
20.97
f1 (ppm)

2n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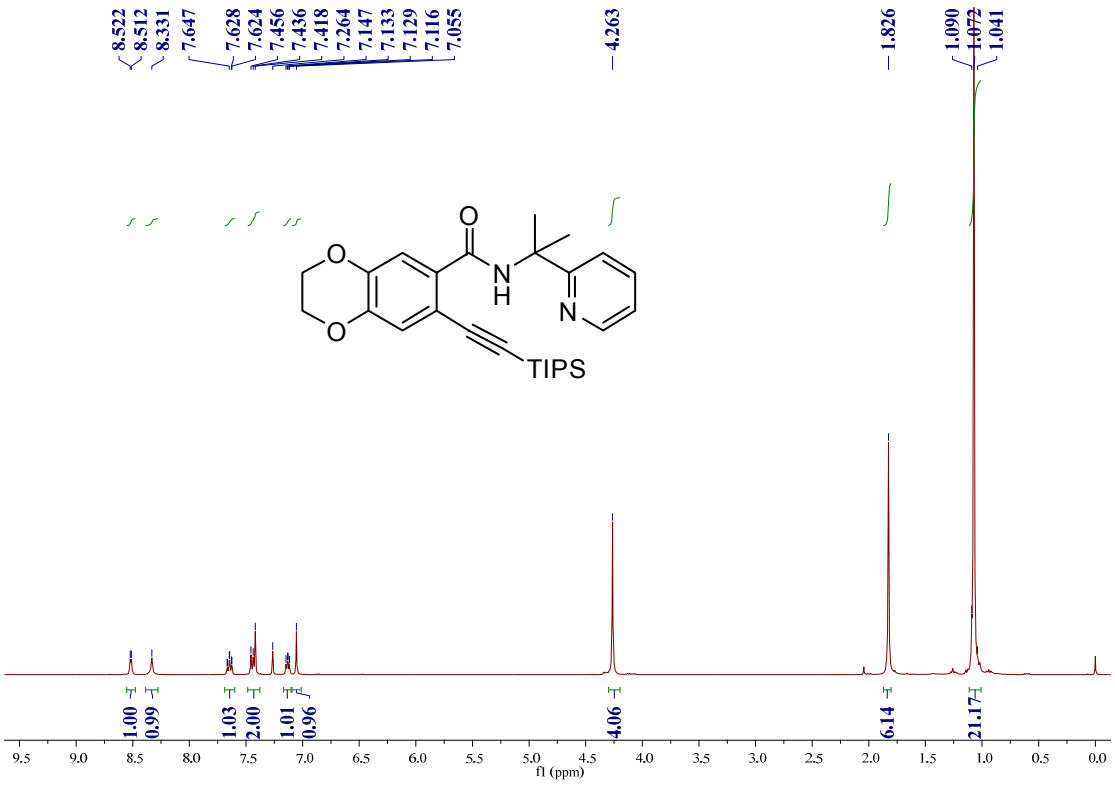
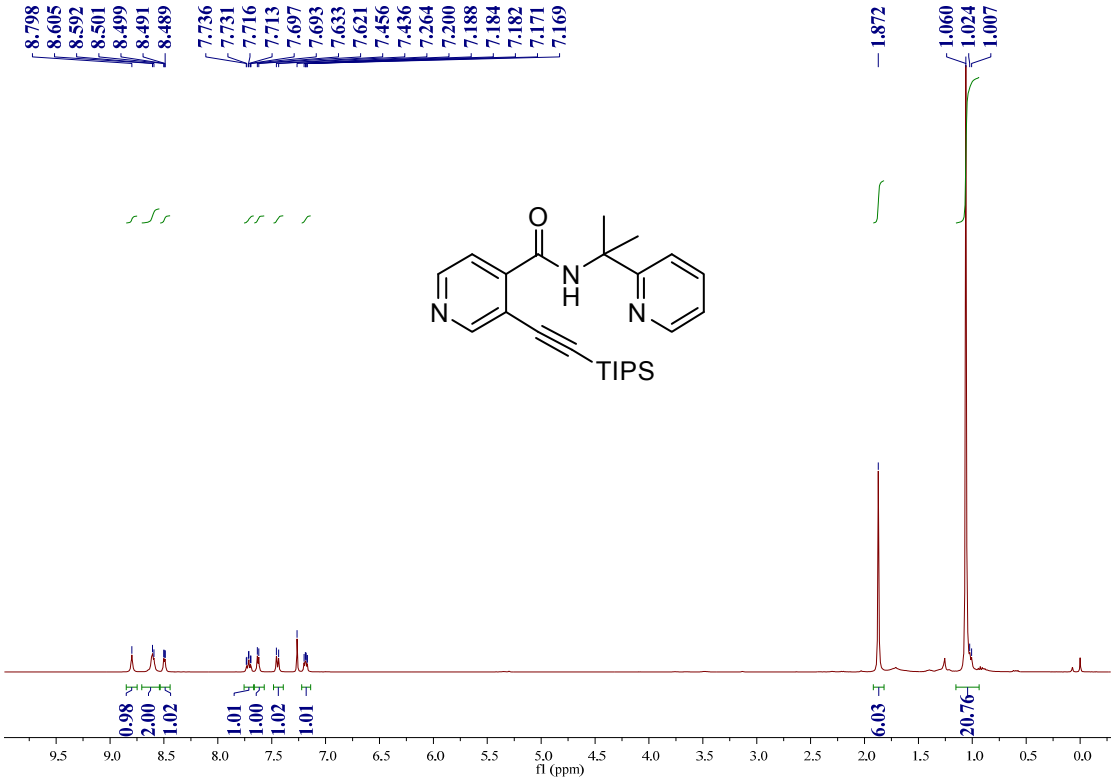
7.036
6.926
6.919
6.904
6.897
3.837
1.842
1.086
1.054
1.033
O
N
H
N
O
TIPS
1.00
0.97
0.99
1.03
1.01
1.03
0.98
1.02
3.00
6.08
21.01
f1 (ppm)

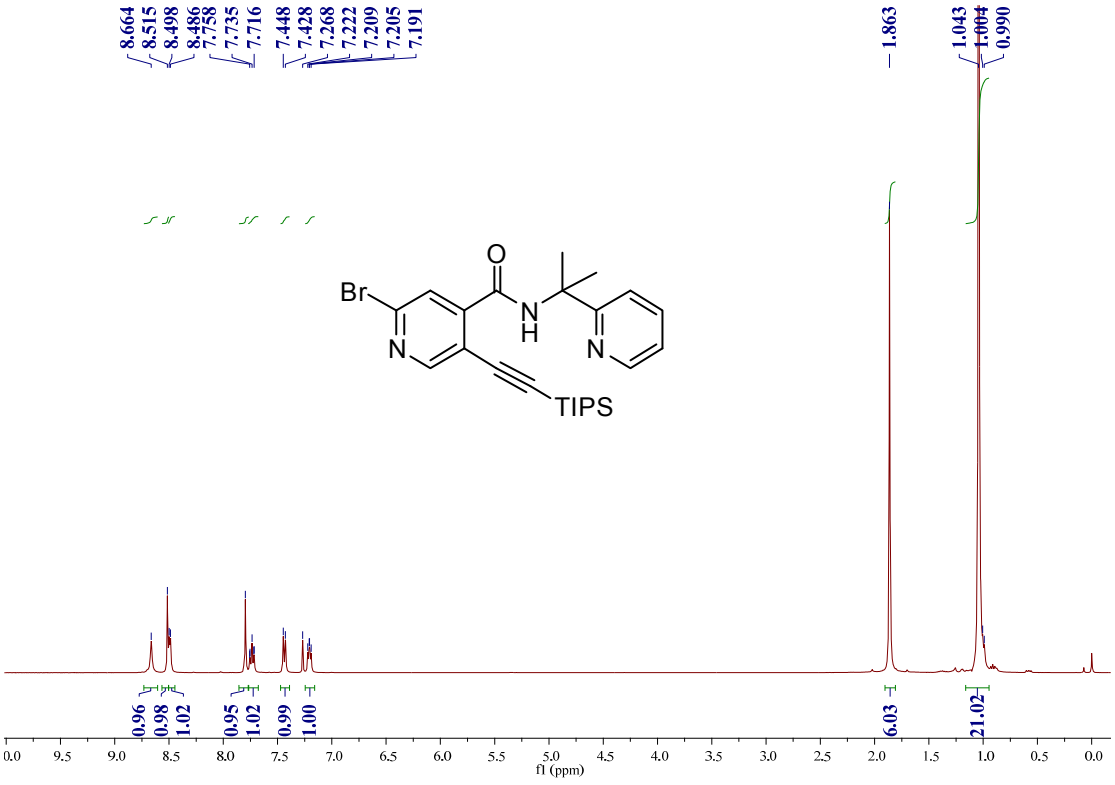
2o


8.522
8.512
8.331
7.647
7.628
7.624
7.456
7.436
7.418
7.264
7.147
7.133
7.129
7.116
7.055
4.263
1.826
1.090
1.072
1.041
O
O
N
H
N
TIPS
1.00
0.99
1.03
2.00
1.01
0.96
4.06
6.14
21.17
f1 (ppm)

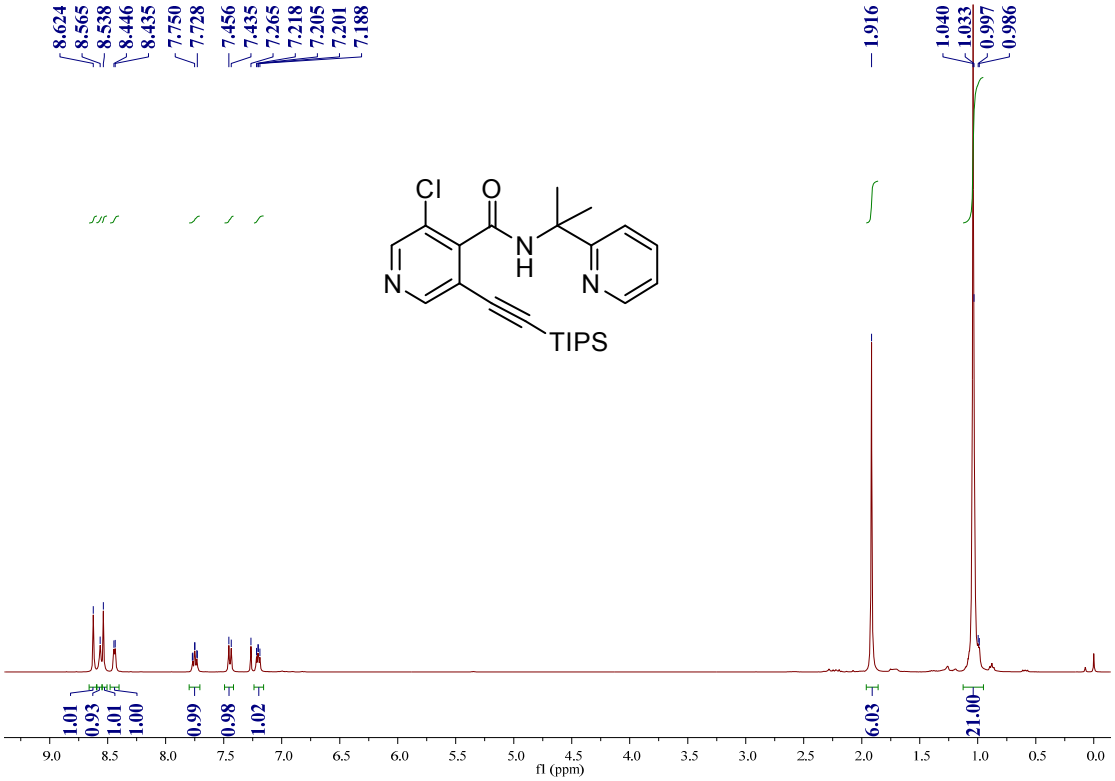
2p


8.798
8.605
8.592
8.501
8.499
8.491
8.489
7.736
7.731
7.716
7.713
7.697
7.693
7.633
7.621
7.456
7.436
7.264
7.200
7.188
7.184
7.182
7.171
7.169
1.872
1.060
1.024
1.007
O
N
H
N
N
TIPS
0.98
2.00
1.02
1.01
1.00
1.02
1.01
6.03
20.76
f1 (ppm)

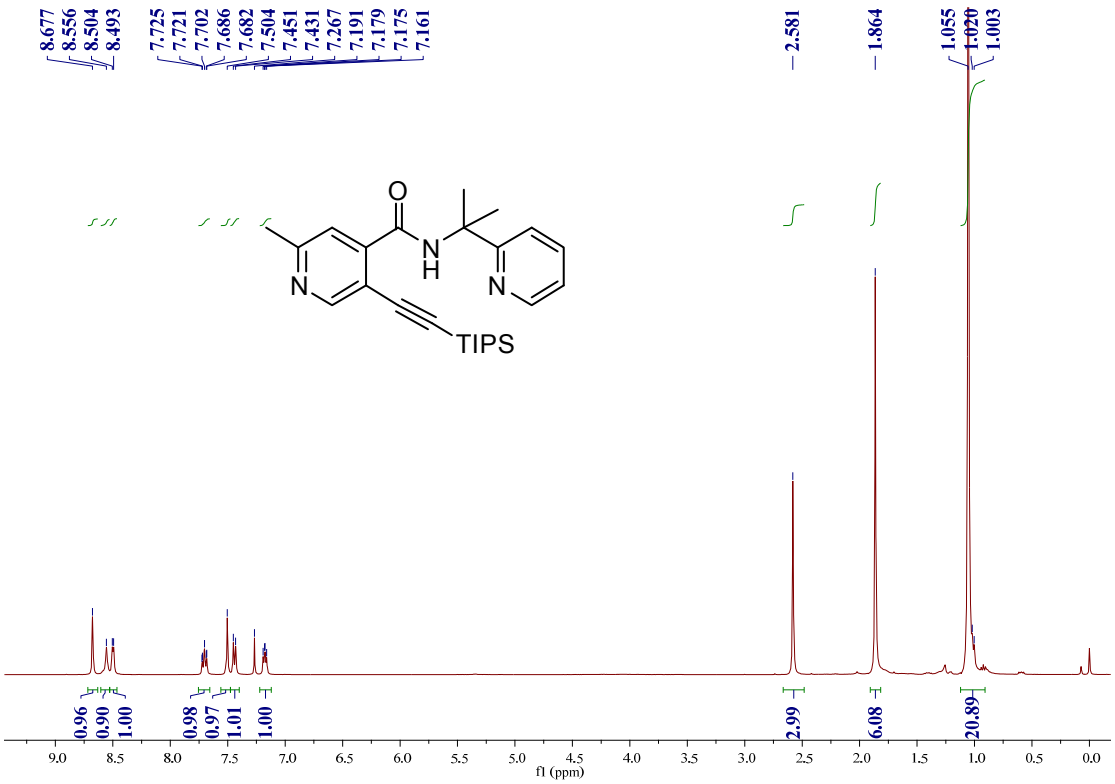
2q


8.664
8.515
8.498
8.486
7.758
7.735
7.716
7.448
7.428
7.268
7.222
7.209
7.205
7.191
1.863
1.043
1.004
0.990
O
Br
N
H
N
N
TIPS
0.96
0.98
1.02
0.95
1.02
0.99
1.00
6.03
21.02
f1 (ppm)

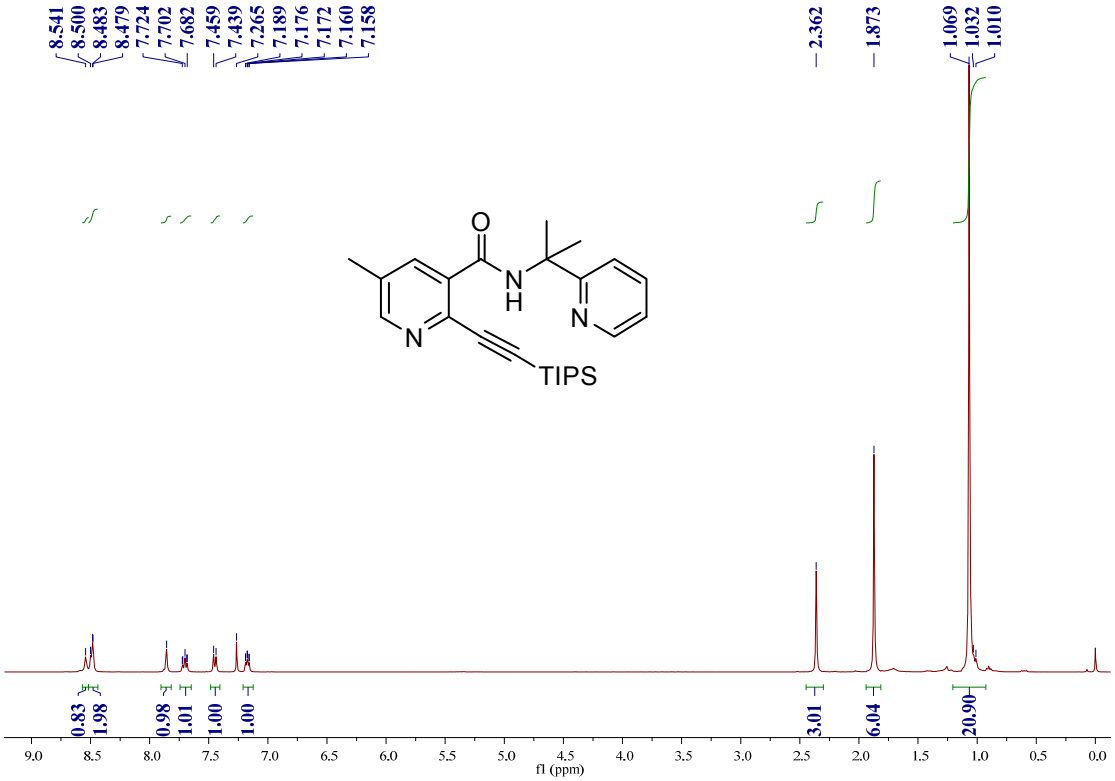
2r


8.624
8.565
8.538
8.446
8.435
7.750
7.728
7.456
7.435
7.265
7.218
7.205
7.201
7.188
1.916
1.040
1.033
0.997
0.986
Cl
O
N
H
N
N
TIPS
1.01
0.93
1.01
1.00
0.99
0.98
1.02
6.03
21.00
f1 (ppm)

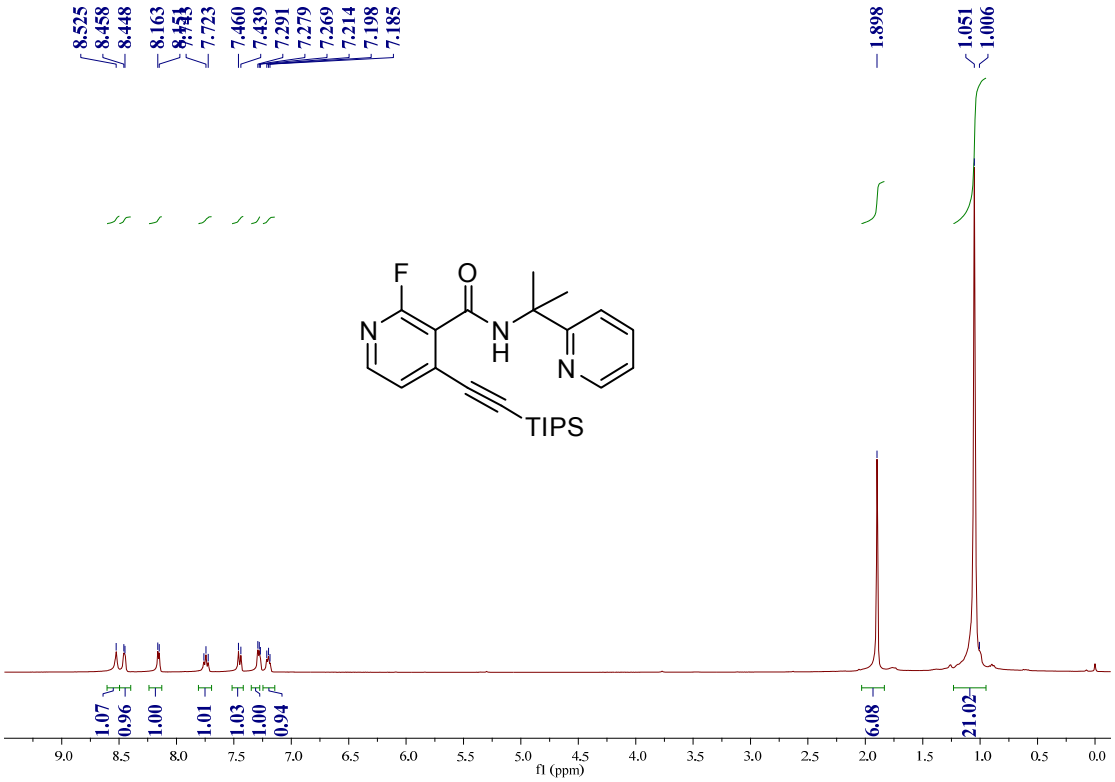
2s

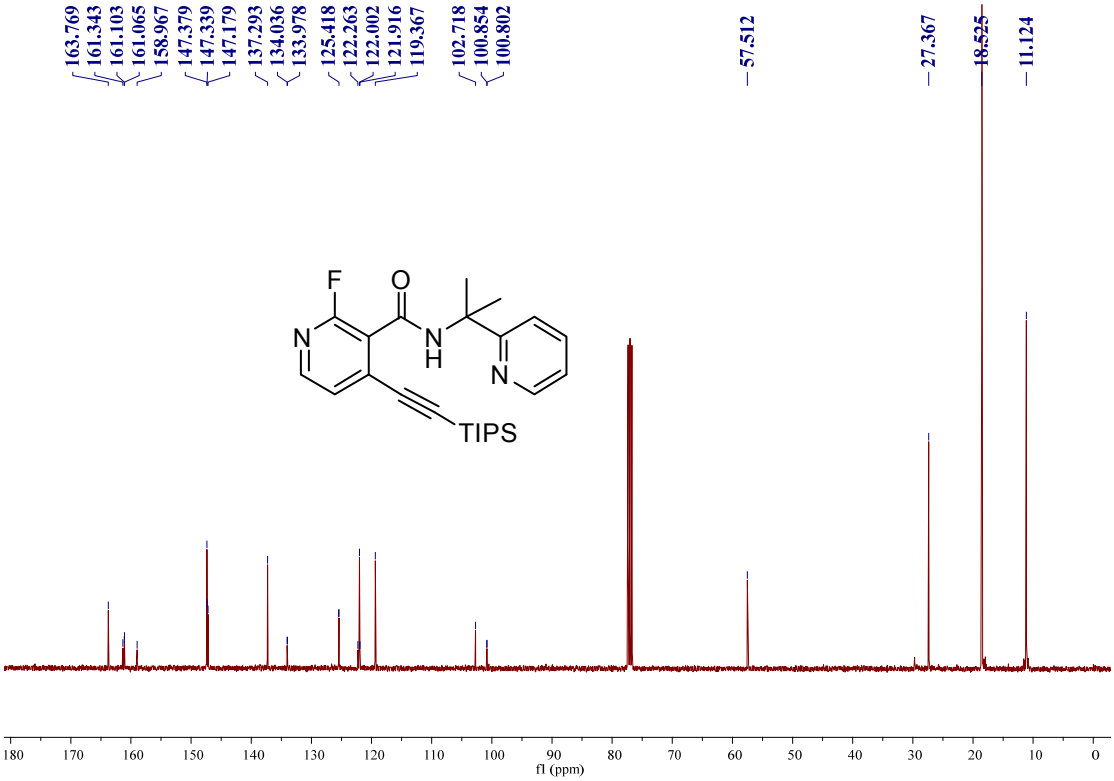

8.677
8.556
8.504
8.493
7.725
7.721
7.702
7.686
7.682
7.504
7.451
7.431
7.267
7.191
7.179
7.175
7.161
2.581
1.864
1.055
1.020
1.003
O
N
H
N
N
TIPS
0.96
0.90
1.00
0.98
0.97
1.01
1.00
2.99
6.08
20.89
f1 (ppm)

2t

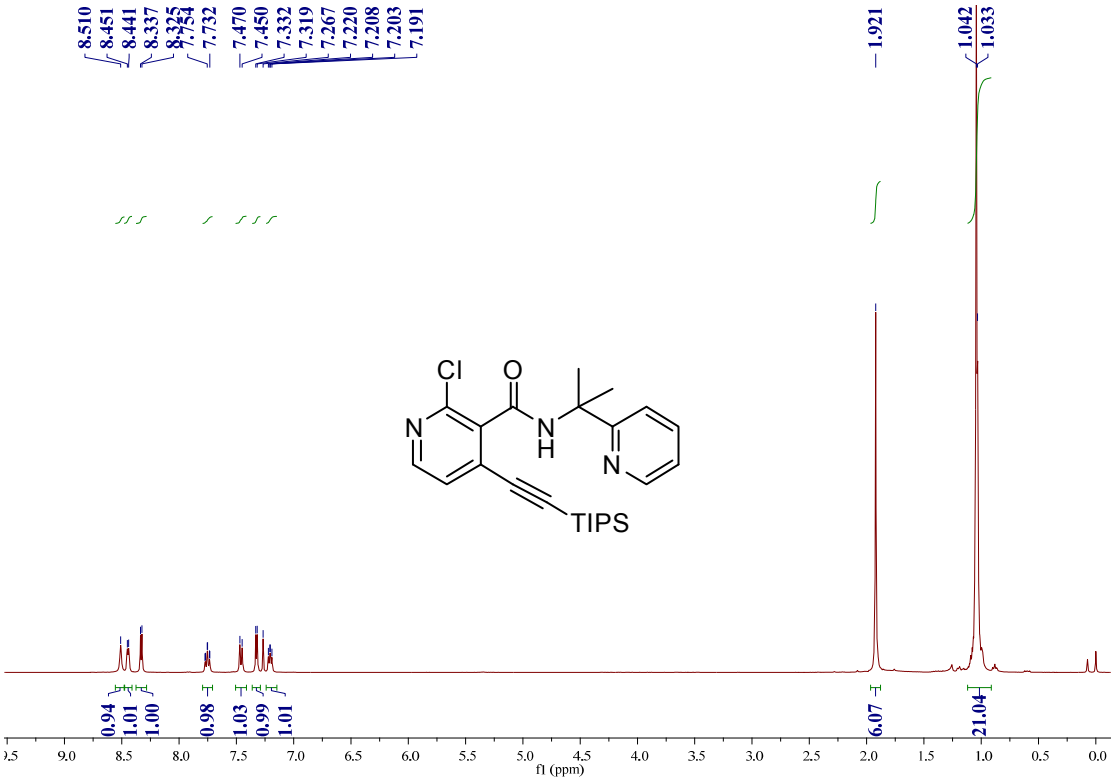

8.541
8.500
8.483
8.479
7.724
7.702
7.682
7.459
7.439
7.265
7.189
7.176
7.172
7.160
7.158
2.362
1.873
1.069
1.032
1.010
O
N
H
N
N
TIPS
0.83
1.98
0.98
1.01
1.00
1.00
3.01
6.04
20.90
f1 (ppm)

2u

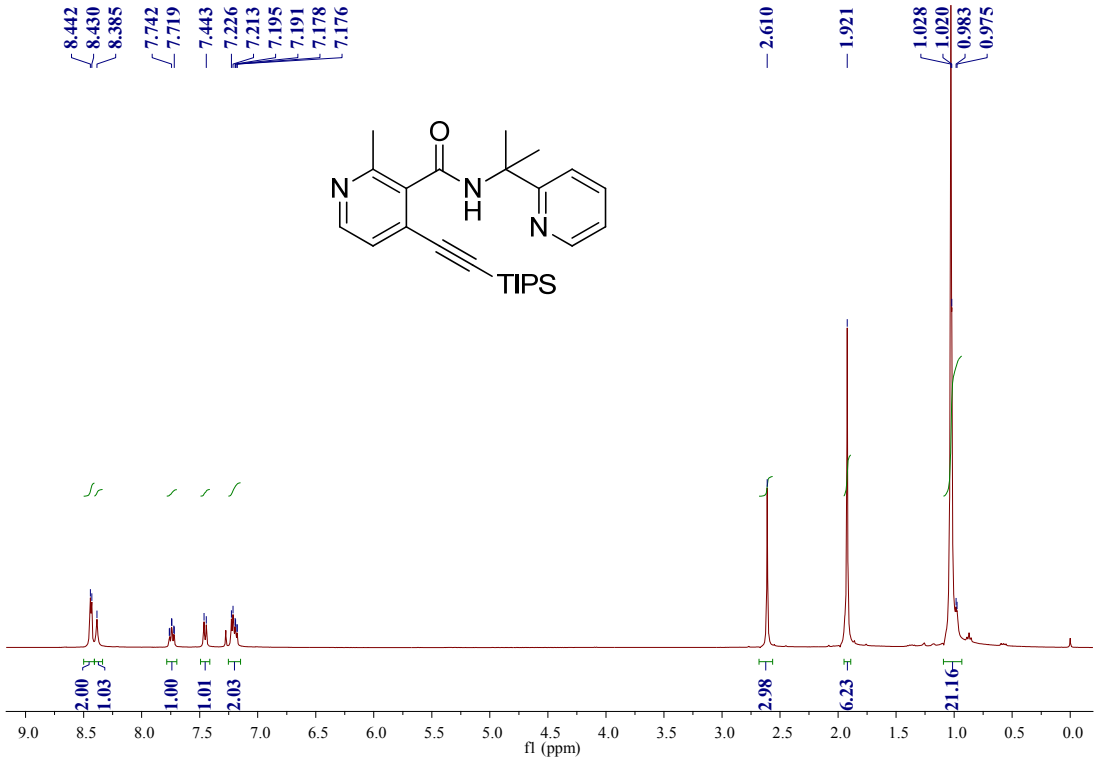

8.525
8.458
8.448
8.163
7.723
7.460
7.439
7.291
7.279
7.269
7.214
7.198
7.185
1.898
1.051
1.006
F
O
N
N
H
N
TIPS
1.07
0.96
1.00
1.01
1.03
1.00
0.94
6.08
21.02
f1 (ppm)

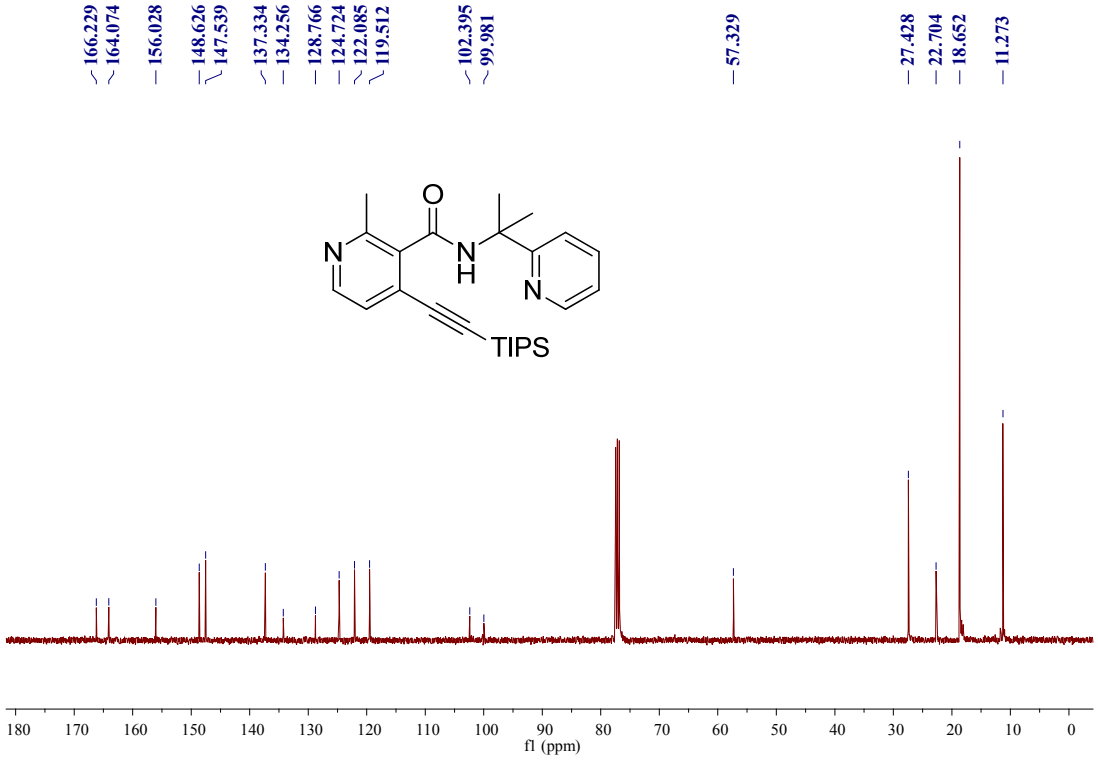

163.769
161.343
161.103
161.065
158.967
147.379
147.339
147.179
137.293
134.036
133.978
125.418
122.263
122.002
121.916
119.367
102.718
100.854
100.802
57.512
27.367
18.525
11.124
F
O
N
H
N
N
TIPS
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

2v

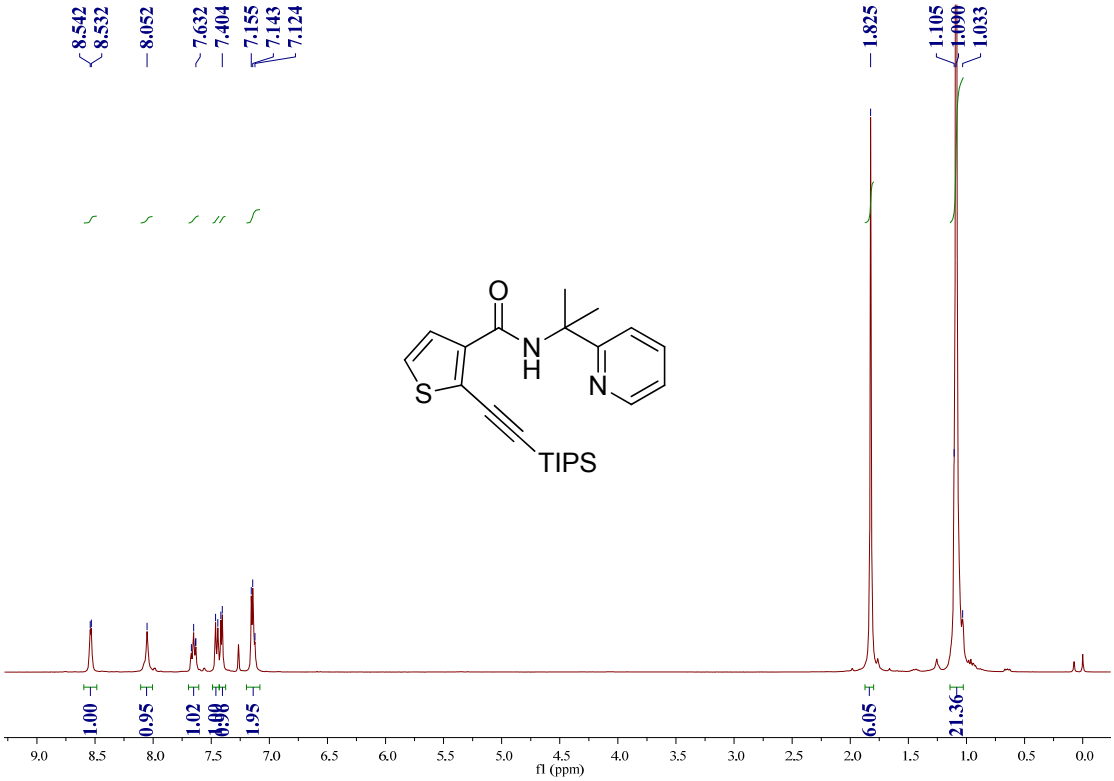

8.510
8.451
8.441
8.337
7.754
7.732
7.470
7.450
7.332
7.319
7.267
7.220
7.208
7.203
7.191
1.921
1.042
1.033
Cl
O
N
H
N
N
TIPS
0.94
1.01
1.00
0.98
1.03
0.99
1.01
6.07
21.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

2w

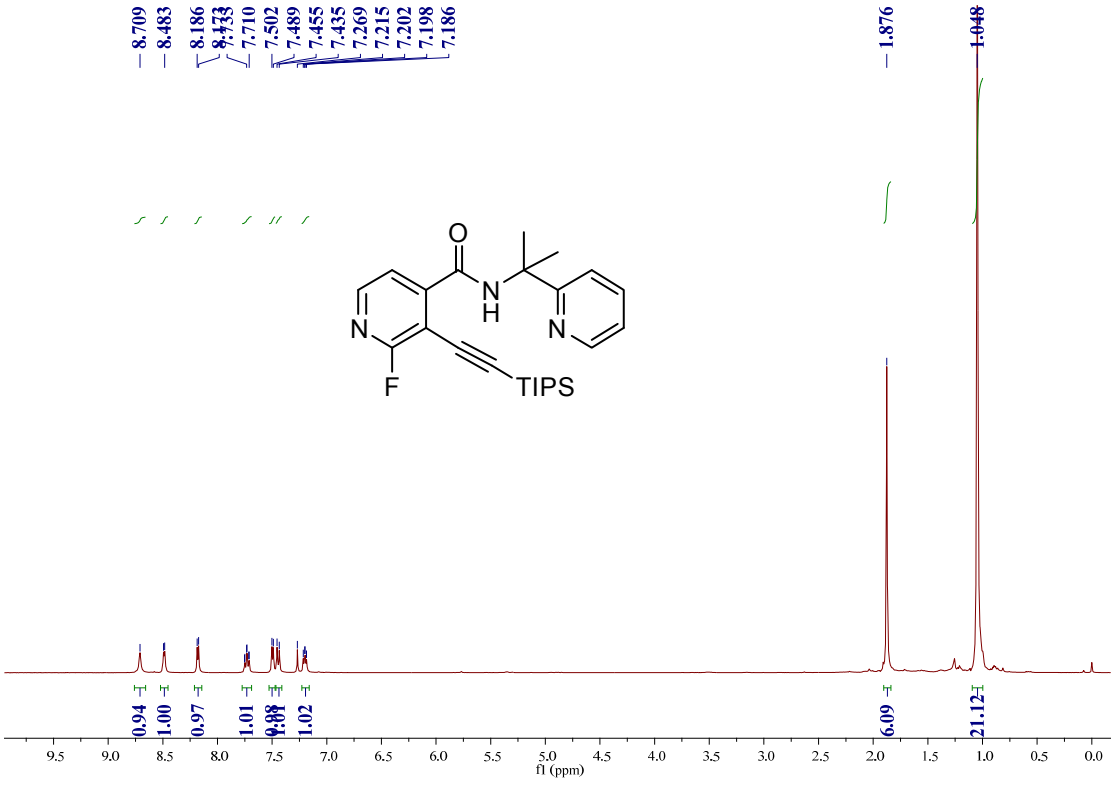

8.442
8.430
8.385
7.742
7.719
7.443
7.226
7.213
7.195
7.191
7.178
7.176
2.610
1.921
1.028
1.020
0.983
0.975
O
N
N
H
N
TIPS
2.00
1.03
1.00
1.01
2.03
2.98
6.23
21.16
fl (ppm)


166.229
164.074
156.028
148.626
147.539
137.334
134.256
128.766
124.724
122.085
119.512
102.395
99.981
57.329
27.428
22.704
18.652
11.273
O
N
N
H
N
TIPS
fl (ppm)

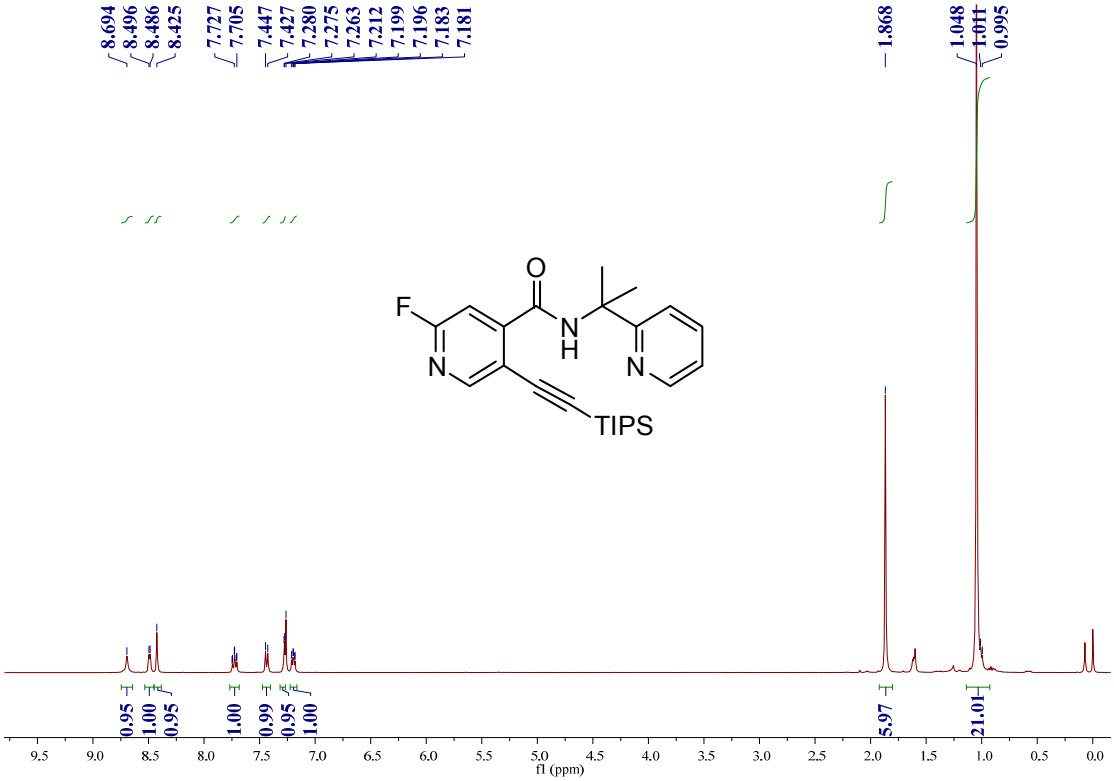
2x

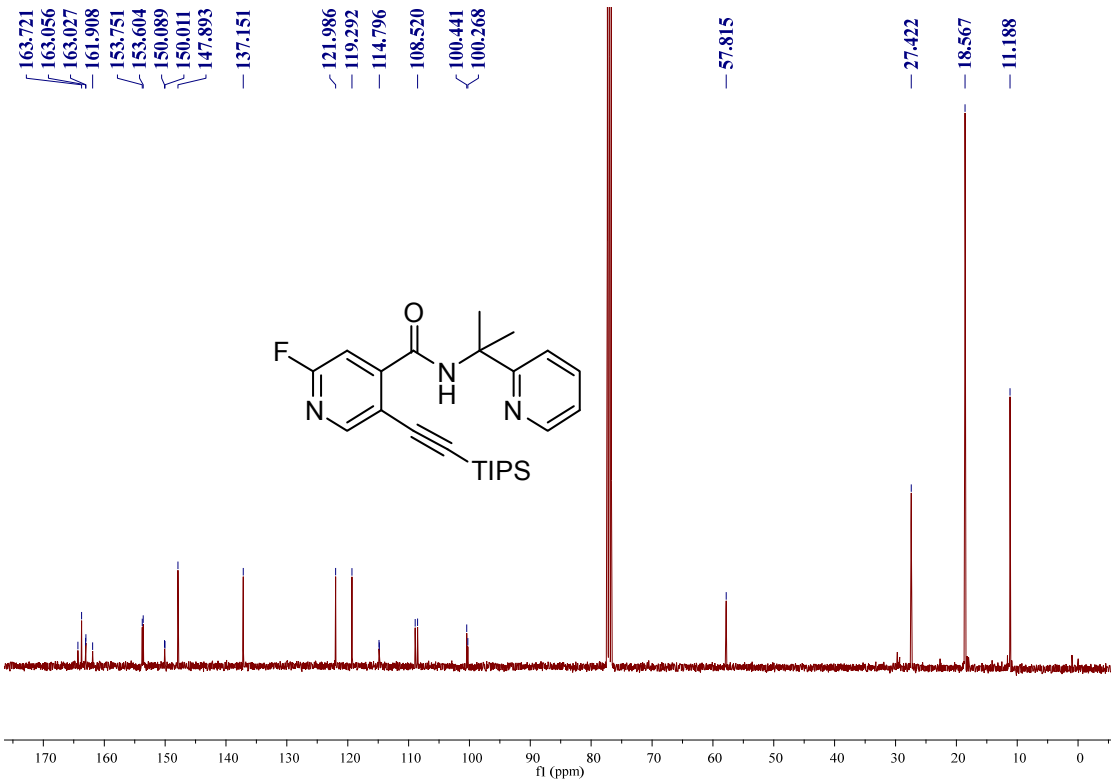

8.542
8.532
8.052
7.632
7.404
7.155
7.143
7.124
1.825
1.105
1.090
1.033
O
N
H
S
N
TIPS
1.00
0.95
1.02
1.95
6.05
21.36
f1 (ppm)

2yb

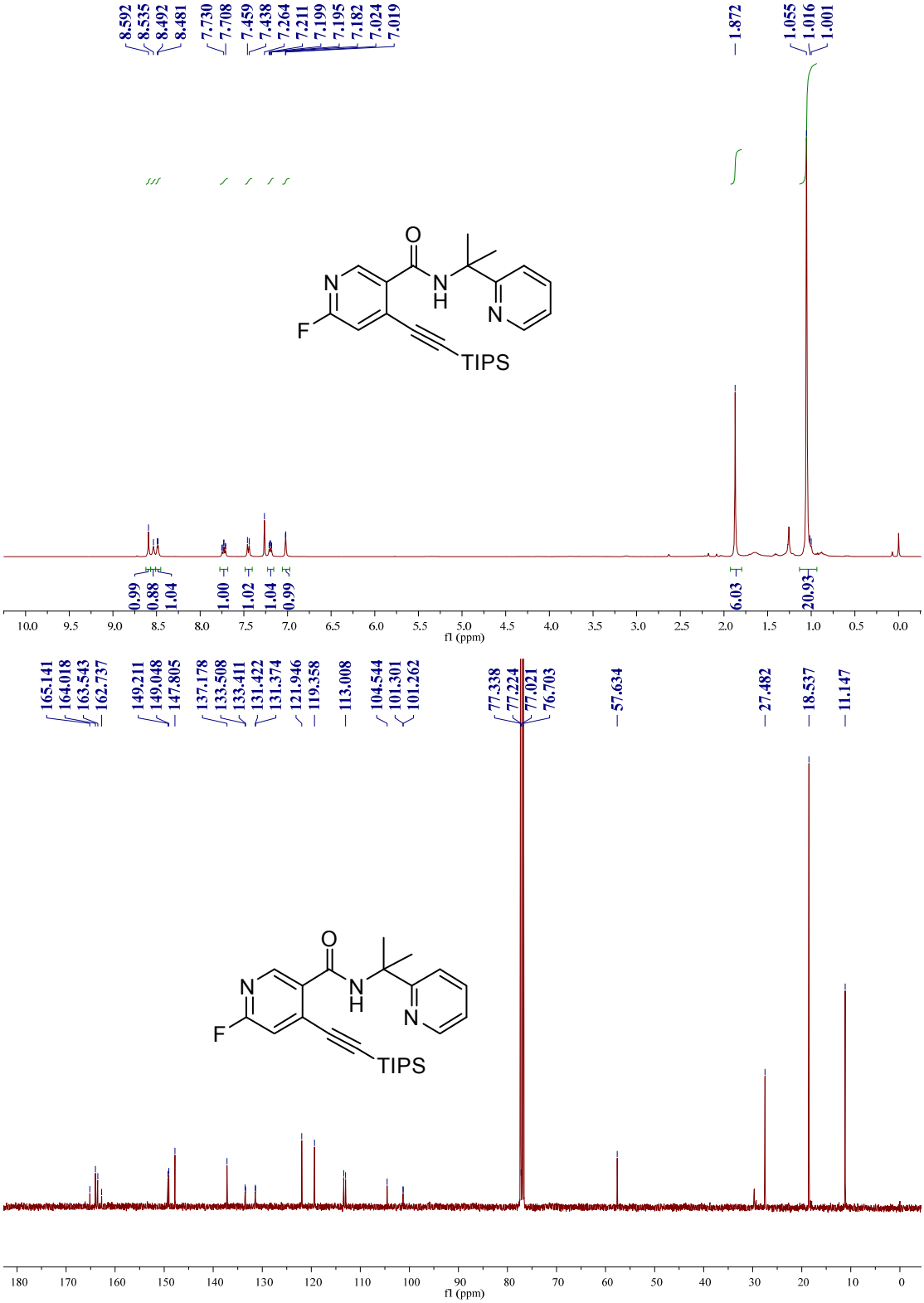

8.709
8.483
8.186
7.710
7.502
7.489
7.455
7.435
7.269
7.215
7.202
7.198
7.186
1.876
1.048
O
N
H
N
N
F
TIPS
0.94
1.00
0.97
1.01
1.02
6.09
21.12
f1 (ppm)

2ya

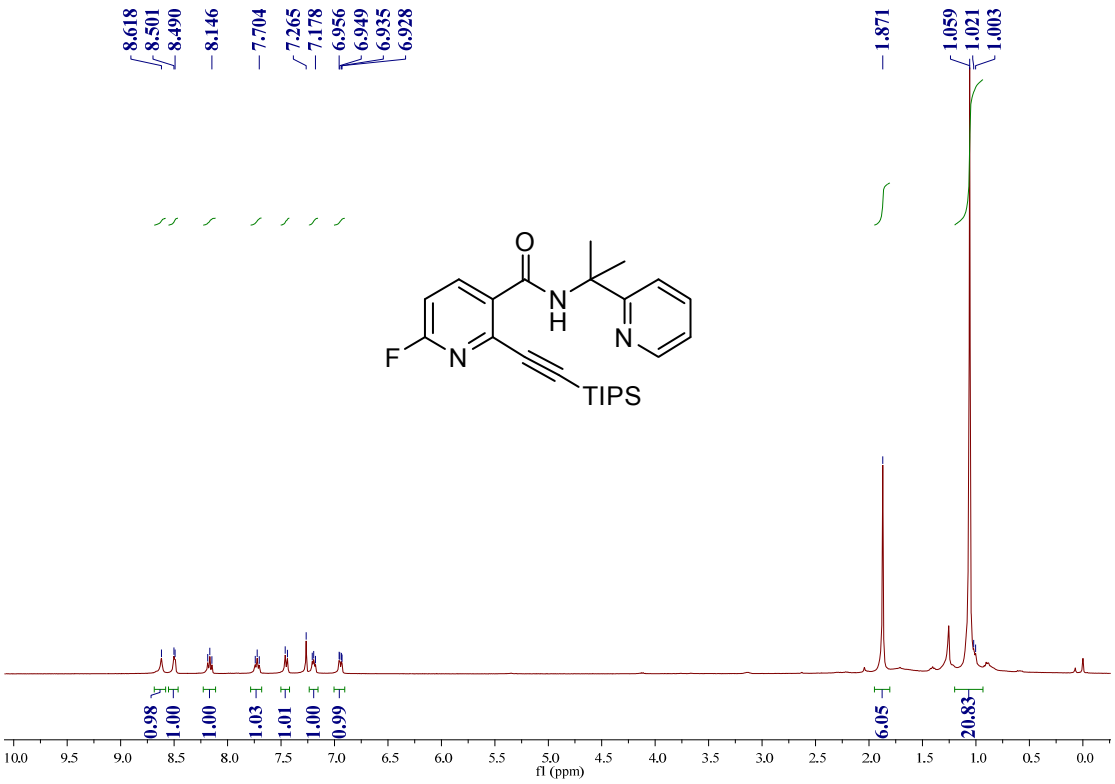

8.694
8.496
8.486
8.425
7.727
7.705
7.447
7.427
7.280
7.275
7.263
7.212
7.199
7.196
7.183
7.181
1.868
1.048
1.011
0.995
O
F
N
H
N
N
TIPS
0.95
1.00
0.95
1.00
0.99
0.95
1.00
5.97
21.01
f1 (ppm)

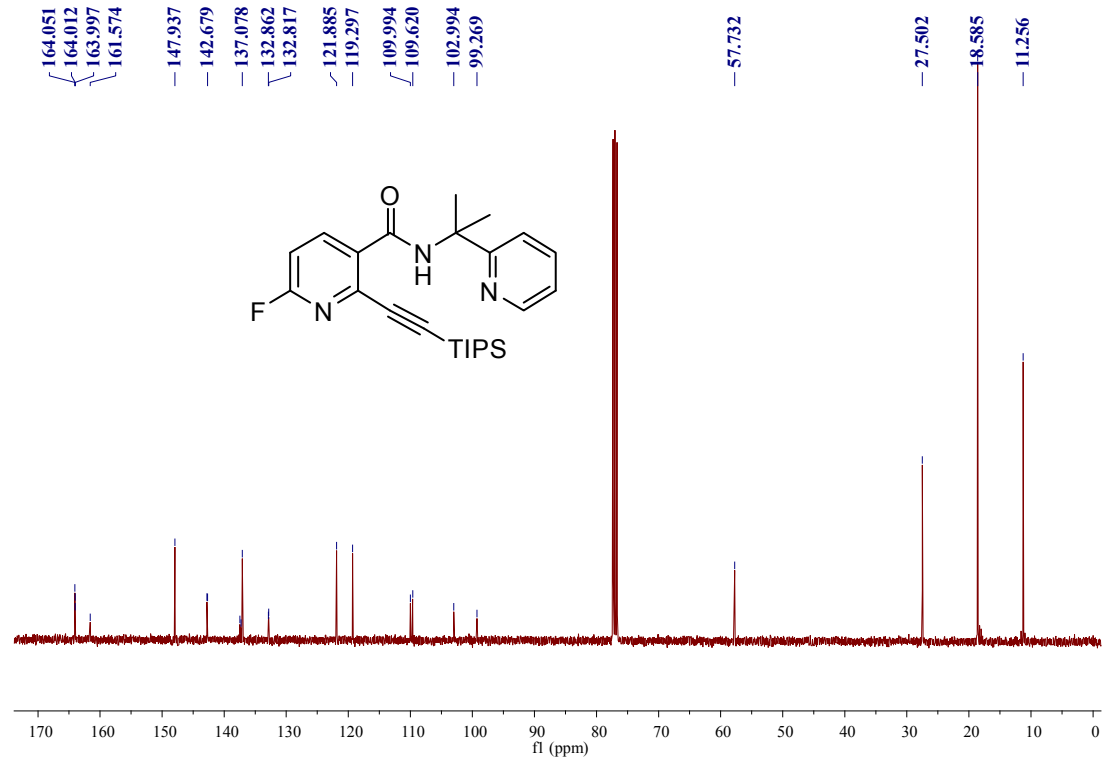

163.721
163.056
163.027
161.908
153.751
153.604
150.089
150.011
147.893
137.151
121.986
119.292
114.796
108.520
100.441
100.268
57.815
27.422
18.567
11.188
O
F
N
H
N
N
TIPS
f1 (ppm)

2za

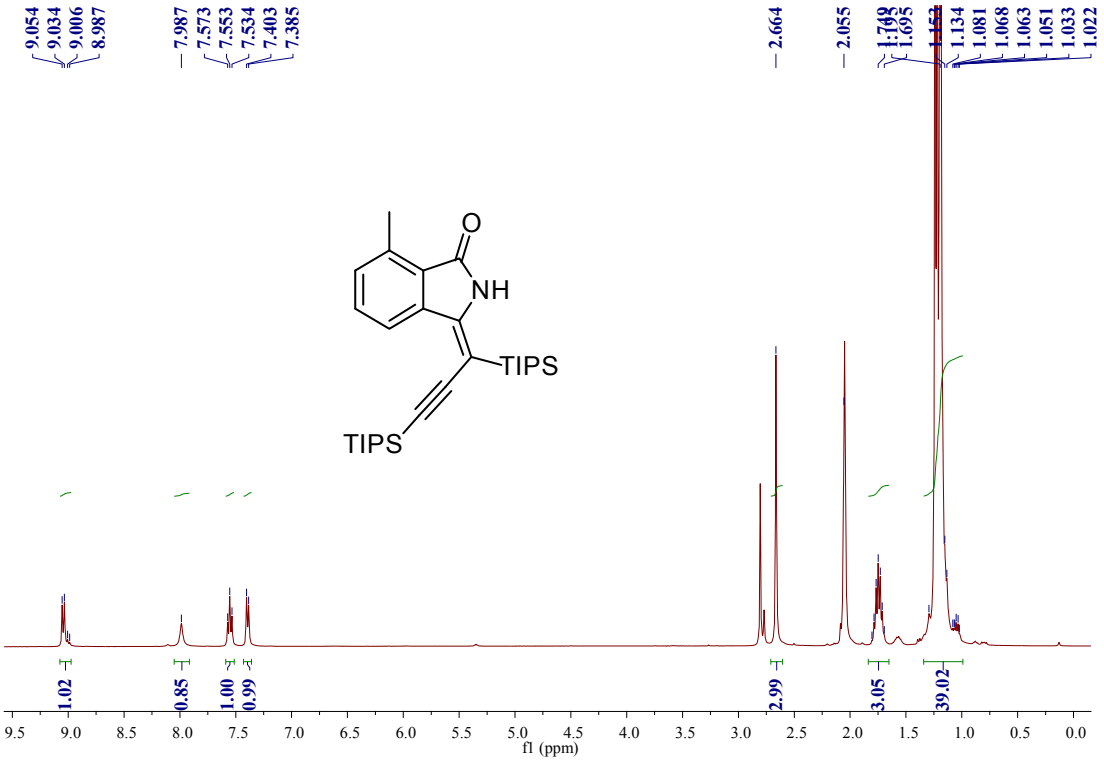

8.592
8.535
8.492
8.481
7.730
7.708
7.459
7.438
7.264
7.211
7.199
7.195
7.182
7.024
7.019
1.872
1.055
1.016
1.001
0.99
0.88
1.04
1.00
1.02
1.04
0.99
6.03
20.93
f1 (ppm)
165.141
164.018
163.543
162.737
149.211
149.048
147.805
137.178
133.508
133.411
131.422
131.374
121.946
119.358
113.008
104.544
101.301
101.262
77.338
77.224
77.021
76.703
57.634
27.482
18.537
11.147
f1 (ppm)

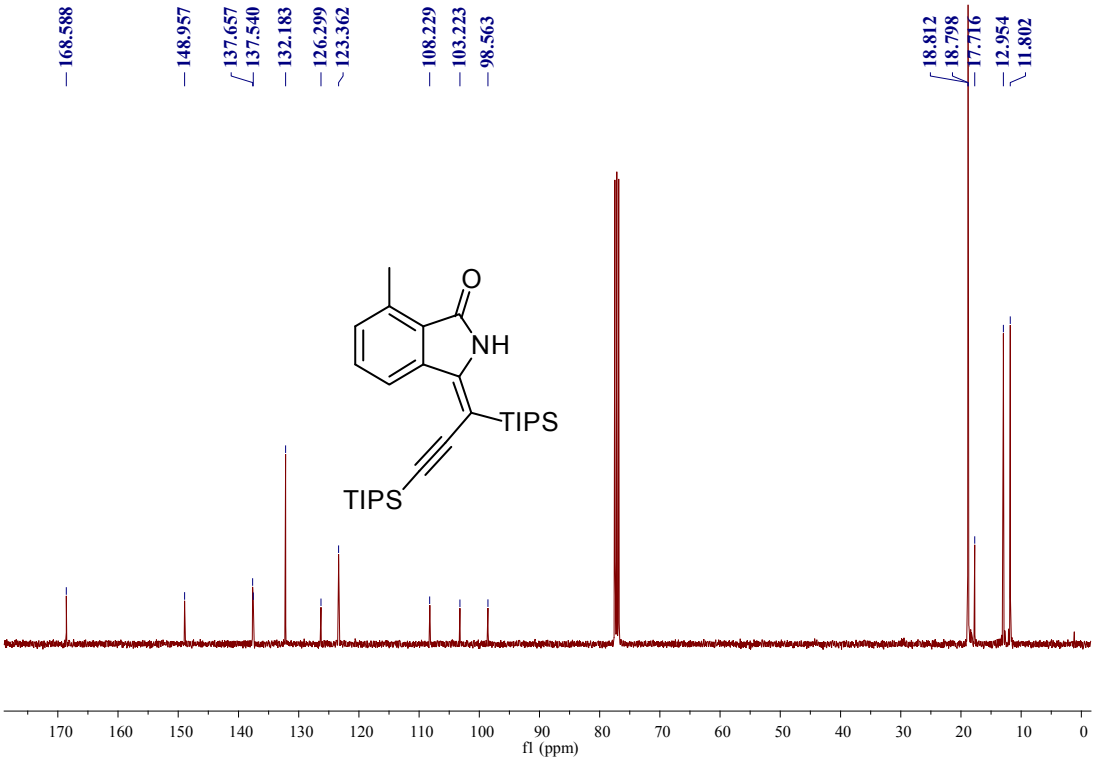
2zb


8.618
8.501
8.490
8.146
7.704
7.265
7.178
6.956
6.949
6.935
6.928
1.871
1.059
1.021
1.003
O
N
H
F
N
N
TIPS
0.98
1.00
1.00
1.03
1.01
1.00
0.99
6.05
20.83
f1 (ppm)

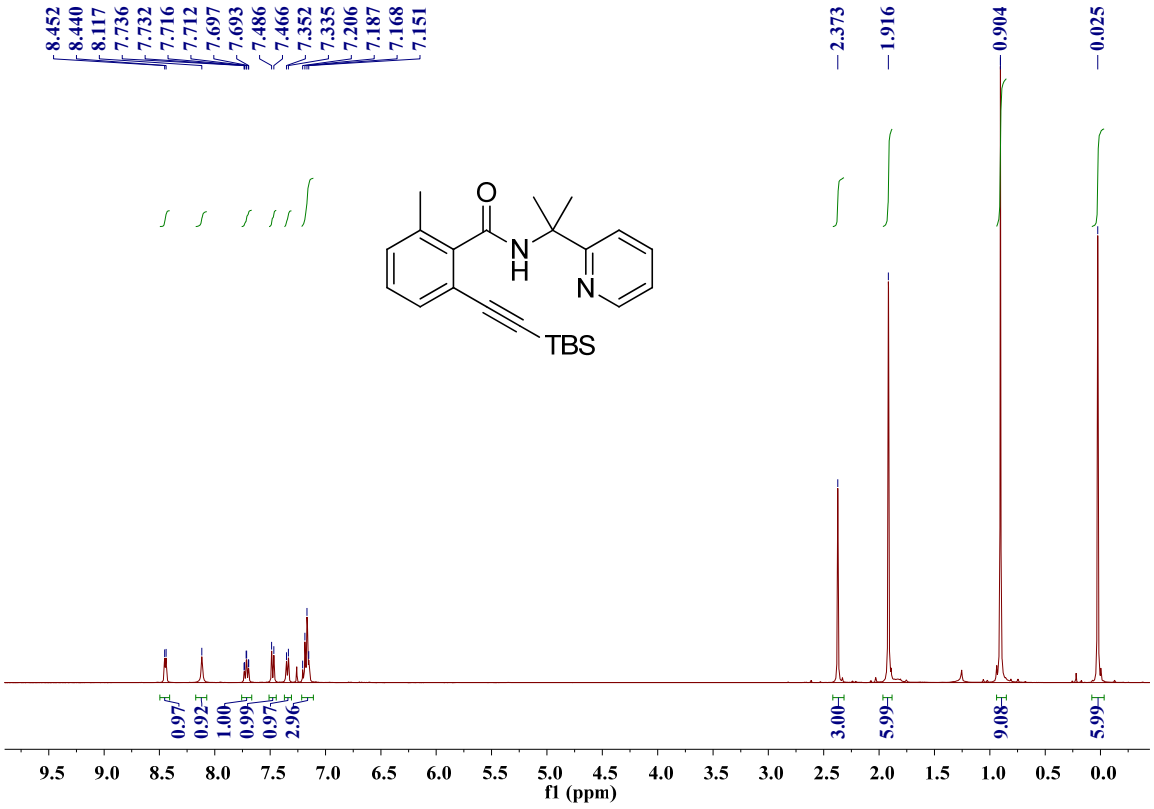

164.051
164.012
163.997
161.574
147.937
142.679
137.078
132.862
132.817
121.885
119.297
109.994
109.620
102.994
99.269
57.732
27.502
18.585
11.256
O
N
H
F
N
N
TIPS
f1 (ppm)

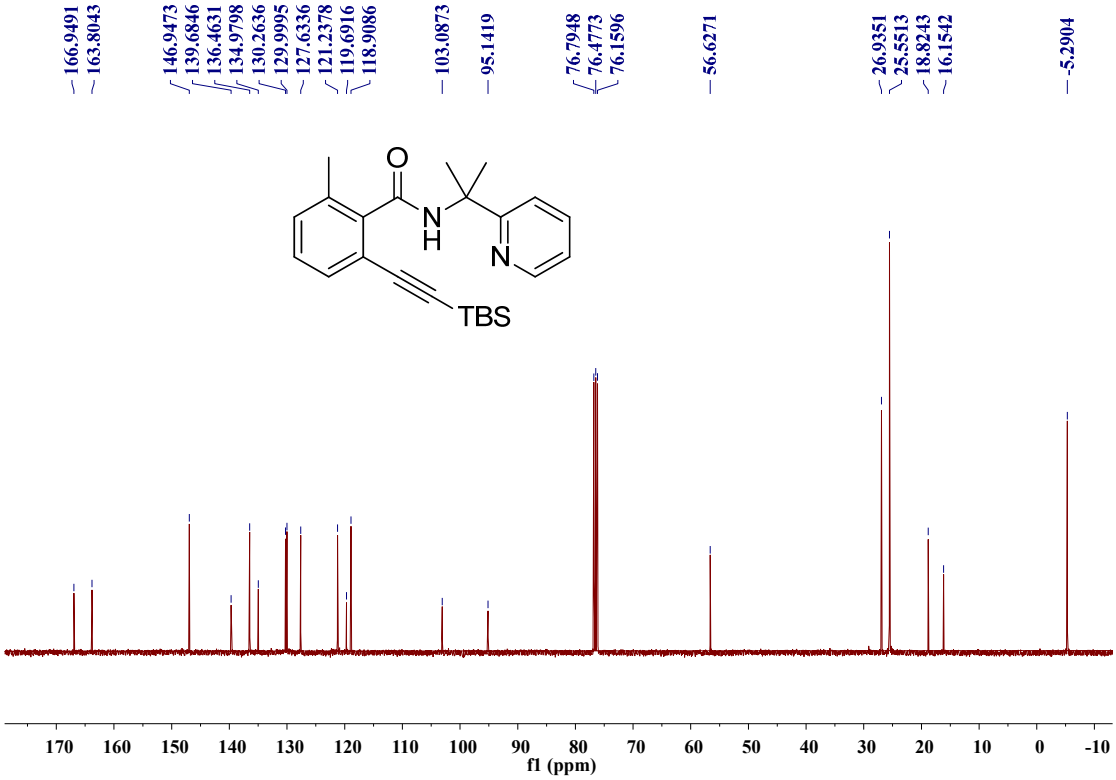
3a


9.054
9.034
9.006
8.987
7.987
7.573
7.553
7.534
7.403
7.385
2.664
2.055
1.749
1.695
1.153
1.134
1.081
1.068
1.063
1.051
1.033
1.022
O
NH
TIPS
TIPS
1.02
0.85
1.00
0.99
2.99
3.05
39.02
fl (ppm)

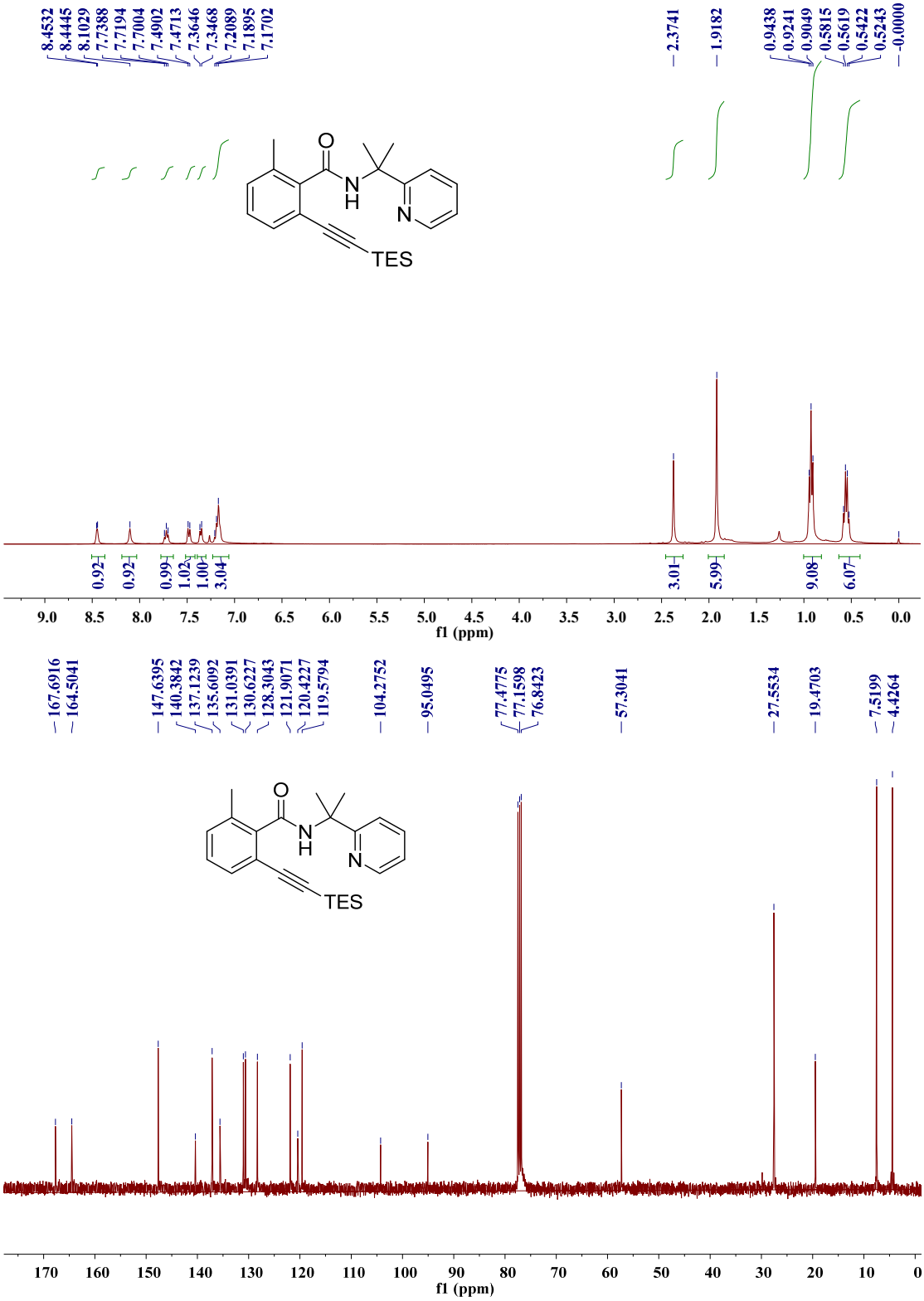

168.588
148.957
137.657
137.540
132.183
126.299
123.362
108.229
103.223
98.563
18.812
18.798
17.716
12.954
11.802
O
NH
TIPS
TIPS
fl (ppm)

4a

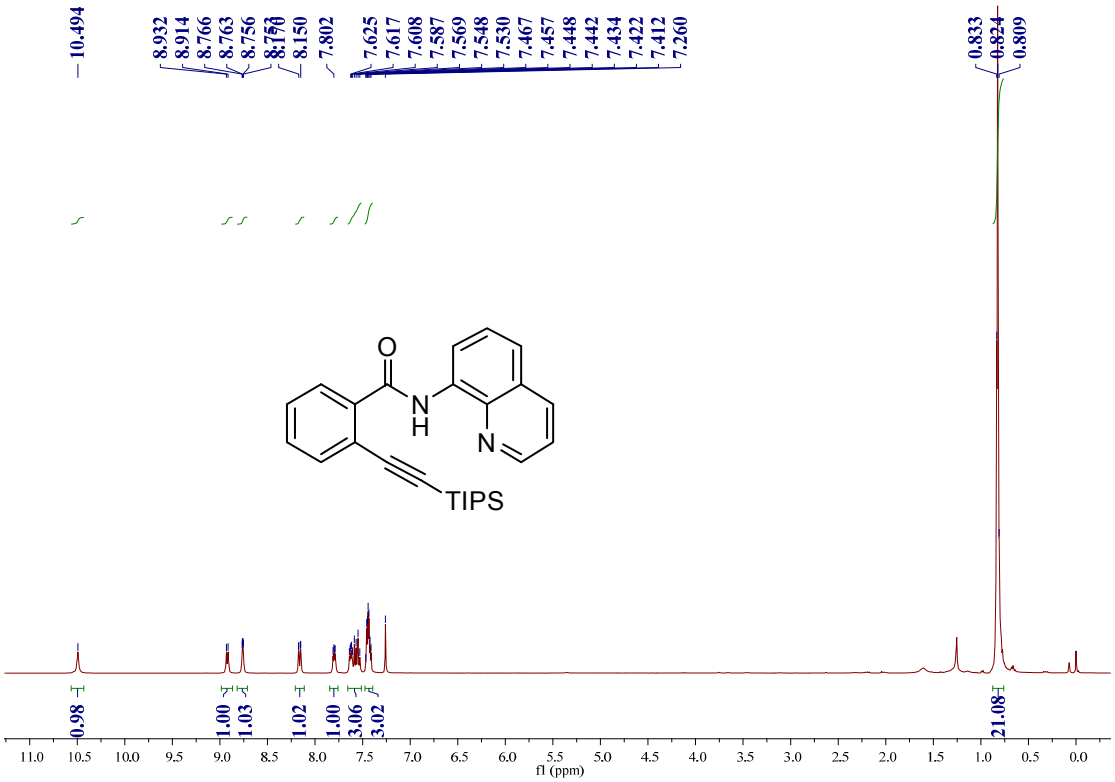

8.452
8.440
8.117
7.736
7.732
7.716
7.712
7.697
7.693
7.486
7.466
7.352
7.335
7.206
7.187
7.168
7.151
2.373
1.916
0.904
0.025
O
N
H
N
TBS
0.97
0.92
1.00
0.99
0.97
2.96
3.00
5.99
9.08
5.99
f1 (ppm)

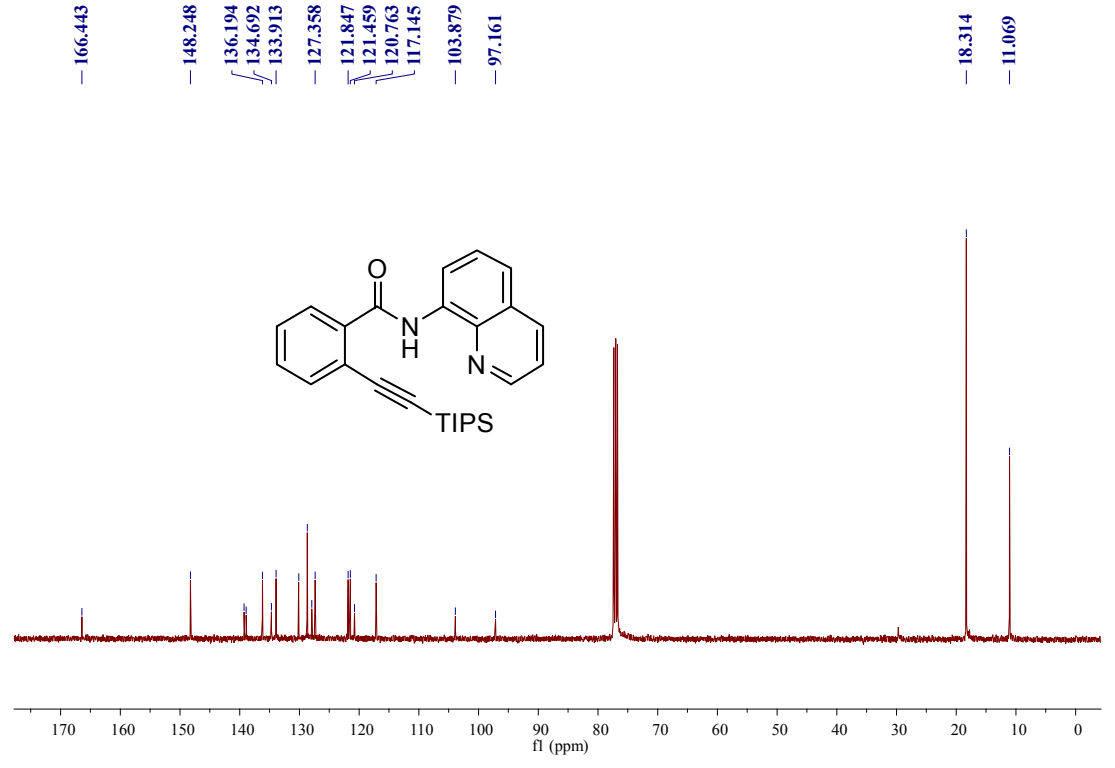

166.9491
163.8043
146.9473
139.6846
136.4631
134.9798
130.2636
129.9995
127.6336
121.2378
119.6916
118.9086
103.0873
95.1419
76.7948
76.4773
76.1596
56.6271
26.9351
25.5513
18.8243
16.1542
-5.2904
O
N
H
N
TBS
f1 (ppm)

4b


8.4532
8.4445
8.1029
7.7388
7.7194
7.7004
7.4902
7.4713
7.3646
7.3468
7.2089
7.1895
7.1702
2.3741
1.9182
0.9438
0.9241
0.9049
0.5815
0.5619
0.5422
0.5243
-0.0000
O
N
H
N
TES
0.92
0.92
0.99
1.02
1.00
3.04
3.01
5.99
9.08
6.07
f1 (ppm)
167.6916
164.5041
147.6395
140.3842
137.1239
135.6092
131.0391
130.6227
128.3043
121.9071
120.4227
119.5794
104.2752
95.0495
77.4775
77.1598
76.8423
57.3041
27.5534
19.4703
7.5199
4.4264
f1 (ppm)

5


10.494
8.932
8.914
8.766
8.763
8.756
8.150
7.802
7.625
7.617
7.608
7.587
7.569
7.548
7.530
7.467
7.457
7.448
7.442
7.434
7.422
7.412
7.260
0.833
0.824
0.809
O
N
H
N
TIPS
0.98
1.00
1.03
1.02
1.00
3.06
3.02
21.08
fl (ppm)


166.443
148.248
136.194
134.692
133.913
127.358
121.847
121.459
120.763
117.145
103.879
97.161
18.314
11.069
O
N
H
N
TIPS
fl (ppm)